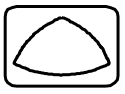


Baptist HRPP/IRB

Standard Operating Procedures

August 2025

Contents

1 Human Research Protection Program

Baptist fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the Organization. In support of this, Baptist has established a Human Research Protection Program (HRPP). The Baptist HRPP, in partnership with its research community, is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under Baptist's auspices.

1.1 Mission

The mission of the HRPP is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- Provide guidance and support to the research community in the conduct of research with human subjects;
- Assist the research community in ensuring compliance with relevant regulations;
- To provide timely and high quality education, review and monitoring of human research projects; and
- To facilitate excellence in human subject research.

The HRPP includes mechanisms to:

- Monitor, evaluate and continually improve the protection of human research participants;
- Dedicate sufficient resources to facilitate excellence and integrity in human research;
- Exercise oversight of research protection;
- Educate investigators and research staff about their ethical responsibility to protect research participants; and
- When appropriate, intervene in research and respond directly to concerns of research participants.

1.2 Organization Authority

Baptist's Human Research Protection Program operates under the authority of the Baptist Institutional Policy, "Human Research Protection Program (HRPP)" adopted on [DATE]. As stated in that policy, the operating procedures in this document "…serve as the governing procedures for the conduct and review of all human research conducted under the auspices of Baptist." The HRPP Policy and these operating procedures are made available to all BMHCC/BHSU/BCRI investigators and research staff and are posted on the HRPP website (www.ORGANIZATION.com).

1.3 Ethical Principles

Baptist is committed to conducting research with the highest regard for the welfare of human subjects. With the exception of transnational research, where consideration of alternative ethical principles may apply, Baptist upholds and adheres to the principles of the Belmont Report by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979). These principles are:

1. Respect for Persons, which involves obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
2. Beneficence, which involves ensuring that possible benefits are maximized and possible risks are minimized to all human subjects.
3. Justice, which involves the equitable selection of subjects.

Baptist HRPP, in partnership with its research community (i.e., researchers and research staff, IRB members and chairs, IRB staff, the organizational official, employees and students) is responsible for ensuring the ethical and equitable treatment of all human subjects in research conducted under its auspices.

1.4 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and organizational policies (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe).

Human subject research at Baptist entities is conducted in accordance with the policy and regulations found in the Common Rule (e.g., 45 CFR 46 Subpart A) and, as applicable, FDA regulations at 21 CFR 50, 21 CFR 56, 21 CFR 312 and 21 CFR 812. NOTE: The Department of Justice (DOJ) is not a signatory to the 2018 Common Rule; as such pre-2018 Common Rule regulations apply to research conducted or supported by this entity.

The actions of Baptist will also conform to any additional regulations as required (e.g., research funded by Department of Defense, Department of Justice, Department of Education-FERPA, PPRA, etc.).

Research involving the use of Protected Health Information is reviewed and conducted in accordance with the Health Insurance Portability and Accountability Act (HIPAA), 45 CFR Part 160, 162, and 164. See Section 26, HIPAA Compliance in Research for details concerning compliance with HIPAA.

1.5 International Conference on Harmonization-Good Clinical Practice (ICH-GCP)

Baptist voluntarily applies the International Conference on Harmonization (ICH) Good Clinical Practices (GCP) Guidelines (sometimes referred to as "ICH-GCP" or "E6") to clinical trials of drugs, only when required by a sponsor or funding agency, and only to the extent that they are compatible with FDA, HHS, and other regulations.

1.6 Federalwide Assurance (FWA)

DHHS regulations require that institutions engaged in non-exempt human subject research that is conducted or supported by any HHS agency file and maintain a Federalwide Assurance with the Office for Human Research Protections (OHRP). An FWA is an organization's assurance to the U.S. government that that non-exempt human subject research is conducted in compliance with federal regulations pertaining to the protection of human subjects. Baptist maintains a FWA on file with OHRP and ensures that it remains current.

An FWA is an organization's assurance to the federal government that human subject research conducted at that site is compliant with federal regulations pertaining to the protection of human subjects.

The FWA designates the internal Institutional Review Board (IRB) that will review and oversee the research, specifies the ethical principles under which the research will be conducted, and names the individuals who will be responsible for the proper conduct of the research.

Baptist has an OHRP-approved Federalwide Assurance (FWA number 00004299) and has designated one IRB to facilitate the conduct of research. The Baptist IRB will keep the IRB membership roster current.

Baptist IRB serves as the Privacy Board for all research conducted under the auspices of Baptist.

The Baptist IRB reviews all research that engages Baptist in the human research activity. Any additional IRBs that review research covered by Baptist's FWA will be confirmed to be registered with OHRP (whether or not they are designated on Baptist's FWA) and a reliance/authorization agreement will be signed between Baptist and the IRB of Record.

In its FWA, Baptist has opted to limit the application of the FWA to non-exempt human subject research conducted or supported by HHS or federal agencies that have adopted the Common Rule. When human subjects research is not subject to the Common Rule or FDA regulations, Baptist ensures that human research subjects benefit from equivalent protections by applying the Common Rule standards, with purposeful deviations that do not meaningfully diminish protections as noted within this manual.

1.7 Research Under the Auspices of the Organization

Research under the auspices of Baptist includes research conducted at Baptist, conducted by or under the direction of any employee or agent of Baptist (including students) in connection with his or her organizational responsibilities, conducted by or under the direction of any employee or agent of Baptist using any property or facility of Baptist, or involving the use of Baptist's non-public information to identify, contact, or study human subjects. The research may be externally funded, funded from internal sources, or conducted without direct funding.

All human subjects research under the auspices of Baptist is under the jurisdiction of the Baptist HRPP. Human subject research that Baptist is engaged in (per OHRP or FDA guidelines) is under the jurisdiction of its IRB, unless Baptist chooses to rely upon another IRB for review and ongoing IRB oversight of the research (the IRB of record for the research).

Employee or Agent of Baptist:

For the purposes of this document, "employees or agents" refers to individuals who:

- act on behalf of the organization;
- exercise organizational authority or responsibility; or
- perform organizationally designated activities.
- "Employees and agents" can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation.

1.8 Engagement in Research

The Department of Health and Human Services (HHS) regulations [45 CFR 46.103[a]] require that an institution "engaged" in human subject research conducted or supported by a Federal Department or Agency provide the Office for Human Research Protection (OHRP) with a satisfactory assurance of compliance with the HHS regulations, unless the research is exempt under 45 CFR 46.101(b) (pre-2018 Common Rule) or 45 CFR 46.104 (2018 Common Rule).

"In general, an institution is considered engaged in a particular non-exempt human subject research project when its employees or agents, for the purposes of the research project, obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research."

The guidance also states that institutions that receive an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subject research (i.e. awardee institutions), are also considered engaged in research even where all activities involving human subjects are carried out by employees or agents of another institution.

FDA regulations are oriented to the responsibilities of IRBs, investigators, and sponsors as opposed to institutions.

When external organizations and researchers wish to conduct research that is under the auspices of Baptist, the external organization or researchers must consult with the Baptist HRPP or IRB staff prior to initiating any research activities at or involving Baptist (See Section 11.4.6.1).

In general, FDA-regulated research conducted in Baptist's facilities or by Baptist's principal or sub-investigators (as defined on the FDA 1572 or delegation of responsibilities log) requires review by a Baptist-designated IRB. Exceptions to this requirement may be granted on a case-by-case basis (e.g., when Baptist's involvement in the research is limited to the provision of a common diagnostic procedure and associated reading or analysis).

An IRB Chair or Vice Chair, with the assistance of the Assistant Director and legal counsel as needed, will determine whether Baptist is to be engaged in a particular research study. Investigators and other institutions may not independently determine whether Baptist is engaged in a particular research study.

When a Baptist entity is to engage in research, the Assistant Director may choose to enter into an agreement to cede review to an external IRB.

For additional information on determining engagement, please refer to OHRP's Guidance on Engagement

on Institutions in Human Subjects Research (Engagement of Institutions in Human Subjects Research (2008)).

1.9 Key Definitions

Human Subject Research. Human Subject Research means any activity that meets the definition of "research" and involves "human subjects" as defined by the Common Rule or other applicable regulations (e.g., FDA).
Note: The terms "subject" and "participant" are used interchangeably in this document and have the same definition.
Minimal Risk. 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 examinations or tests.

Common Rule. The Common Rule refers to the "Federal Policy for the Protection of Human Subjects" adopted by a number of federal agencies. Although the Common Rule is codified by each agency separately, the text is identical to DHHS regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Clinical Trial. Per the 2018 Common Rule and NIH Policy, clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. FDA regulations refer to "clinical investigations" (see definition of "research" below).

Human Subject. A human subject as defined by the Common Rule is a living individual about whom an investigator conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR 46.102(e)(1)].

Human Subject (FDA). Human subject means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. A subject might be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used or tested or used as a control (regardless of whether the specimens are identifiable). [21 CFR 50.3(g), 21 CFR 312.3(b), 21 CFR 812.3(p)].

Intervention means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. [45 CFR 46.102(e)(2)].

Interaction means communication or interpersonal contact between investigator and subject. Please note that per OHRP interaction includes indirect means of communication such as via completion of a web-based survey.

Private information means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

Identifiable private information means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. [45 CFR 46.102(e)(5)]. Note: This definition is within the 2018 Common Rule. For a discussion of identifiability under HIPAA, please see Section 27.

Identifiable biospecimen means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen [45 CFR 46.102(e)(6)]

Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

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 examinations or tests.

Protected Health Information (PHI): Individually identifiable health information:

1) Except as provided in paragraph (2) of this definition, that is:
    a) Transmitted by electronic media;
    b) Maintained in electronic media; or
    c) Transmitted or maintained in any other form or medium.
2) Protected health information excludes individually identifiable health information:
    a) In education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g;
    b) In records described at 20 U.S.C. 1232g(a)(4)(B)(iv);
    c) In employment records held by a covered entity in its role as employer; and
    d) Regarding a person who has been deceased for more than 50 years.

Public health authority means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

Research. The Common Rule defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. Activities which meet this definition constitute research whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

Research (FDA). The FDA has defined "research" as being synonymous with the term "clinical investigation." A clinical investigation, as defined by FDA regulations, means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]

Not Research. According to the Common Rule, the following activities are deemed not to be research:

> (1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
>
> (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority*. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
>
> (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. [45 CFR 46.102(l)]
>
> *NIH issues determinations about whether NIH-supported or conducted activities qualify as public health surveillance activities deemed to be "not research" under the revised Common Rule.

Investigators and institutions may not make their own determinations.

Systematic investigation. For the purposes of these policies and procedures, a "systematic investigation" is an activity that involves a study plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a study question.

Generalizable knowledge. Knowledge gained from a study that may be applied to populations outside of the specific study population, inform policy, or generalize findings. In accordance with OHRP guidance, the establishment of a research repository is also considered a systematic investigation intended to develop generalizable knowledge.

Test Article. Test article means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act [42 U.S.C. 262 and 263b-263n]. [21 CFR 50.3(j)]

Test articles covered under the FDA regulations include, but are not limited to:

1. **Human drugs** – A drug is defined as a substance recognized by an official pharmacopoeia or formulary; a substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; a substance (other than food) intended to affect the structure or any function of the body; a substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process). The primary intended use of a drug product is achieved through chemical action or by being metabolized by the body.

2. **Devices** - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o)." The 21st Century Cures Act amended the FD&C Act to specifically exclude certain software functions from the definition of medical device. Summarized, these include exclusions for software functions intended for administrative support of a health care facility; for maintaining or encouraging a healthy lifestyle; to serve as electronic patient records; for transferring, storing, converting formats, or displaying clinical laboratory tests or other device data and results and related information; and for displaying, analyzing, or printing medical information, for supporting or providing recommendations to a health care professional, and enabling the health care professional to independently review the basis for such recommendations. Additional information regarding the application of these exclusions is available on FDA's "Guidance with Digital Health Content" website.

3. **Human Cells, Tissues, or Cellular or Tissue-based Products (HCT/P's)** – HCT/P's means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.

   The following articles are not considered HCT/P's: vascularized human organs for transplantation; whole blood or blood components or blood derivative products subject to listing under parts 607 and 207, respectively; secreted or extracted human products, such as milk, collagen, and cell factors; except that semen is considered an HCT/P; minimally manipulated bone marrow for homologous use and not combined with another article (except for water, crystalloids, or a sterilizing, preserving, or storage agent, if the addition of the agent does not raise new clinical safety concerns with respect to the bone marrow); ancillary products used in the manufacture of HCT/P; cells, tissues, and organs derived from animals other than humans; in vitro diagnostic products as defined in 809.3(a); blood vessels recovered with an organ, as defined in 42 CFR 121.2, that are intended for use in organ transplantation and labeled "For use in organ transplantation only."

4. **Biological Products** - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.

5. **Dietary Supplements** – A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains one or more "dietary ingredients." The "dietary ingredients" in these products may include vitamins, minerals, herbs or other botanicals, amino acids, and other substances found in the human diet, such as enzymes. When a dietary supplement meets the definition of drug, it is regulated as such.

6. **Medical Foods** – A medical food, as defined in section 5(b) of the Orphan Drug Act (21 U.S.C. 360ee (b) (3)), is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

7. **Mobile Medical Apps** - Mobile apps are software applications that can be executed on a mobile platform or a web-based software application that is tailored to a mobile platform but is executed on a server. Mobile medical apps are a subset of mobile apps that medical devices that meet the definition of a medical device and either are intended to be used as an accessory to a regulated medical device; or to transform a mobile platform into a regulated medical device.

8. **Radioactive Drugs** – The term radioactive drug means any substance defined as a drug which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or

photons and includes any nonradioactive reagent kit or nuclide generator which is intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides. The term "radioactive drug" includes "radioactive biological product".

9. **Radiation-Emitting Electronic Products** - a radiation-emitting electronic product as any electrically-powered product that can emit any form of radiation on the electromagnetic spectrum. These include a variety of medical and non-medical products such as mammography devices, magnetic resonance imaging (MRI) devices, laser toys, laser pointers, liquid crystal displays (LCDs), and light emitting diodes (LEDs).

1.10 Written Policies and Procedures

These Standard Operating Procedures (SOPs) for Human Research Protection detail the policies and regulations governing research with human subjects and the requirements for submitting research proposals for review by the Baptist IRB or one of the affiliated IRB's of record, if applicable. This is not a static document and is reviewed every three years or as needed and revised by the Institutional Official and the Assistant Director. The Institutional Official and Assistant Director will approve all revisions of the policies and procedures.

The Institutional Official, through the Assistant Director, will keep the Organization research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists.

The SOPs will be available on the IRB website, and in Baptist HRPP Operations Policy, Procedure and Guideline Manual. Changes to the policies and procedures are communicated to investigators, research staff, and IRB members and IRB staff through training sessions and announcements on the IRB website. In the event of an emergency or disaster (e.g., public health or weather-related), the procedures in the HRPP policies may be modified as appropriate for the situation. Such modifications may include alternative meeting procedures, alternative procedures for the submission and review of modifications, alternative procedures for prompt reporting, and any other changes necessary to ensure appropriate ongoing oversight and conduct of research. Because procedural modifications may vary based on the nature of the event, these cannot be anticipated and described in these policies. Instead, such procedural modifications will be recorded in an addendum to the policies, note-to-file, or other appropriate means of documentation and communicated to the research community. This documentation will be maintained in accordance with applicable record retention requirements.

1.11 HRPP Structure for All Baptist Entities

HRPP consists of various individuals and committees that are responsible for maintaining the HRPP objectives. This consists of Institutional Official, the Assistant Director, the Assistant Director of the HRPP, the Corporate Compliance Officer, the Privacy Officer, the IRB staff, the IRB, Conflict of Interest Committee, Legal Counsel, investigators, research staff, health and safety staff, and research pharmacy staff.

The objective of this system is to assist the organization in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

The following officials, administrative units and individuals have primary responsibilities for human subject protections:

1.11.1 Institutional Official (IO)

The ultimate responsibility of the HRPP resides with the IO of the research program. The IO is legally authorized to represent Baptist, is the signatory of the FWA and assumes the obligations of the FWA.

At Baptist, the President of the Physician Enterprise and Chief Executive Officer of the Baptist Medical Group (BMG) is the Institutional Official.

The IO is responsible for ensuring that Baptist HRPP and IRB have the resources and support necessary to comply with all organizational policies, laws, and regulations that govern human subject research. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program; Appropriate office space, meeting space, equipment, materials, and technology;
- Resources for production, maintenance, and secure storage of HRPP and IRB records;
- Resources for auditing and other compliance activities and investigation of non-compliance; Supporting the implementation of Program decisions and taking administrative actions to ensure compliance.
- Access to legal counsel;
- Supporting educational opportunities related to human research protections for IRB members, relevant administrative staff, and all members of the research team;
- Support for evaluation of Conflict of Interest; and
- Support for Community Outreach.

The IO conducts and documents an annual review of HRPP and IRB function, requirements, and resources and makes adjustments as needed. The adequacy of personnel and non-personnel resources of the HRPP is assessed on an annual basis by the Assistant Director and are reviewed and approved by the IO.

The IO has the authority to suspend, terminate, or disapprove the Institution's approval of research or take other actions, such as sanctions or restrictions of research privileges or uses of research data, as necessary, to ensure the proper conduct of research, the protection of human subjects, the autonomy and authority of the IRB, compliance with regulatory and other requirements, or to protect the interests of Baptist. However, the IO may not approve research that has been disapproved (or not yet approved) by the IRB.

The resources provided for the IRB and the HRPP will be reviewed during the annual budget review process. The IO is also responsible for:

- Fostering, supporting and maintaining an organizational culture that supports the ethical conduct

of all research involving human subjects and the adherence to regulations and organizational policies; Ensuring that the IRB functions independently by, among other mechanisms, being directly accessible to the IRB Chairs and members if they experience undue influence or if they have concerns about the function of the IRB;

- Oversight of the IRB;
- Oversight over the conduct of research conducted under the auspices of Baptist;
- Assuring the IRB members are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations;
- Assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations; and
- Oversight of the development and implementation of an educational plan for IRB members, staff and investigators.

The IO must complete the OHRP Human Subject Assurance Training and training on human research protections available from Collaborative Institutional Training Initiative (CITI).

The IO must complete the OHRP Human Subject Assurance Training and training on human research protections available from Collaborative Institutional Training Initiative (CITI). The HRPP Office will provide on-going continuing education for the IO concerning human research protections.
The designated IO is made known to employees of the organization and is accessible by phone, email, in person or other methods of communication. The IRB Chair and Assistant Director have access to the IO for any concerns or issues related to the HRPP. In the performance of these duties, the IO has the authority to delegate such activities as may be necessary in order to effectively administer the program. However, the IO is ultimately responsible and is expected to be knowledgeable about all human subject protections responsibilities at the organization.

1.11.2 The Assistant Director

The Assistant Director has operational responsibility for the Human Research Protection Program and provides guidance to the IRBs in developing policies and procedures, interpreting regulations, and executing recommendations of senior leadership and governing boards of Baptist. The Assistant Director and the IRB Chairs jointly advise the Institutional Official on appointments to the IRBs.

The Assistant Director confers frequently with the IRB staff and Chairs to evaluate day-to-day needs and can, within certain limits, adjust resources allocated to the HRPP as needed.

The Assistant Director is responsible for:

- Assuring that the HRPP and IRB have appropriate resources to carry out their functions.
- In the third quarter of the fiscal year (or more frequently if necessary), the Assistant Director evaluates the following areas:
    - Space. IRB staff are consulted regarding the adequacy of their personal work spaces, resources for

copying documents; and space to store paper files.

- Personnel. IRB staff are consulted regarding adequacy of staff to respond to programmatic needs. Part of this evaluation will include comparison of workload in the previous year to other years; timeliness and thoroughness of reviews; assessment of matters that had to be deferred because of scarcity of resources.

- HRPP Education Program. IRB staff and members are consulted about their perceptions of the need for training, especially in light of new and more complex protocols that have been presented for review and for continuing "refresher" training in basic principles of human research protections. Additional topics include training on new software for managing IRB operations.

- Legal Counsel. IRB chairs, members and staff are queried regarding their perceptions of need for increased access to legal advice regarding the application of the regulations to specific situations that come before the boards.

- Conflict of Interest. IRB members queried regarding their perceptions of how the conflict of interest disclosure is functioning; whether they understand its various components; and whether it should be modified.

- Membership. IRB members and chairs are consulted regarding the adequacy of the membership to evaluate protocols coming before the boards for review. Among the factors to be considered are scientific expertise and representational capacity of members.

- Developing the annual budget for the IRB. The Assistant Director presents his/her findings to the IRB at a convened meeting in the fourth quarter of the fiscal year, and recommendations will be incorporated into the IRB budget request, which is developed in the second quarter.

- The Assistant Director is responsible for coordinating plans for outreach activities to inform the Baptist community as well as the general public about the role of the IRB and the Baptist human research protection program and for evaluating these activities annually. Planning and evaluation will include consultation with IRB members and the Corporate Communications Department. Results of the review will be discussed with IRB members at a convened meeting.
- The job performance of the Assistant Director is evaluated on a yearly basis by the IO. An integral part of the evaluation process is giving constructive feedback to address any performance areas that are deficient or should be improved. If necessary, formal improvement plans are developed, implemented and reviewed at pre-specified intervals.

1.11.3 IRB Coordinator

The IRB Coordinator is expected to be knowledgeable about regulations pertaining to human research protections and be a resource for investigators and their research teams, especially those who may be inexperienced in clinical research, about IRB requirements and human subject protections.

The Coordinator is also responsible for:

- receiving, docketing, and appropriately processing all submissions to the IRB;

- preparing correspondence on behalf of the IRB;
- coordinating and executing meetings of the convened IRB;
- taking minutes of IRB meetings and distributing them to members;
- ensuring compliance with and the documentation of HRPP training requirements; and
- maintaining IRB documents in accordance with all applicable regulatory and institutional retention policies.

The job performance of the IRB Coordinators is evaluated on a yearly basis by the Assistant Director of the HRPP using the Baptist Employee Performance Evaluation. An integral part of the evaluation process is giving constructive feedback to address any performance areas that are deficient or should be improved. If necessary, formal improvement plans are developed, implemented and reviewed at pre-specified intervals.

1.11.4 Institutional Review Board (IRB) (see also Section 9)

Baptist has one IRB appointed by the IO. The IRB prospectively reviews and makes decisions concerning all human research conducted at Baptist facilities, by its employees or agents, or under its auspices unless another IRB has been designated to do so.

The IRB is responsible for the protection of rights and welfare of human research subjects at the Baptist and its affiliates, through review and oversight of safe and ethical research. It discharges this duty by complying with the requirements of federal and state regulations, the FWA, and organizational policies.

The IRB functions independently of, but in coordination with, other organizational committees and officials. The IRB, however, makes its independent determination whether to approve, require modifications in, or disapprove a research plan based upon whether or not human subjects are protected adequately.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the organization. However, those officials may not approve human research that has not been approved or has been disapproved by the IRB.
Baptist also uses the services of WCG IRB for the review of biosafety research, the National Cancer Institute (NCI) Cooperative IRB (CIRB) for oncology cooperative research, and the National Institutes of Health (NIH) sIRB for the review of NIH-funded multi-site studies. WCG IRB is registered with OHRP as IRB00000533; the NCI IRBs are registered as IRBs 00000781, 00009430, 00004296, and 00010018; and the NIH sIRBs are registered as IRB00011862 and IRB00012078. Baptist may enter into reliance agreements for other reasons, for example, when required as a term or condition of a grant.

1.11.5 Legal Counsel

The Baptist HRPP relies on the General Counsel for the interpretations and applications of state law and the laws of any other jurisdiction where research is conducted as they apply to human subject research. General Counsel will also advise the IRB about other legal issues such as who is a child, and who can serve as a legally authorized representative or guardian.

When there are any conflicts between federal or national law and other applicable laws, the General Counsel will determine the appropriate resolution.
All research documents (agreements, contracts, informed consents, etc.) require Legal review and approval prior to execution.

1.11.6 Investigators

The investigator is ultimately responsible for the protection of the human subjects who participate in research and is expected to abide by the highest ethical standards when developing a research plan that incorporates the principles of the Belmont Report.

The investigator is expected to conduct research in accordance with the IRB approved research plan and to oversee all aspects of the research by providing training and supervision of support staff, including oversight of the informed consent process. All subjects must give informed consent unless the requirement has specifically been waived by the IRB. Investigators must establish and maintain an open line of communication with research subjects within their responsibility.

In addition to complying with all applicable policies and standards of regulatory bodies, investigators must comply with organizational and administrative requirements for conducting research.

The investigator is responsible for ensuring that all research staff complete all organizational required training as well as training for their responsibilities in any given specific research study.
When investigational drugs or devices are used, the investigator is responsible for providing a plan for their storage, security, dispensing, accounting, and disposal.

1.11.7 Baptist Clinical Research Institute (BCRI)

Under the BCRI, staff review all research agreements with all sponsors including federal, foundation, and non-profit sponsors. This review ensures that all terms of the award (grant or contract) are in compliance with organizational policies. Only designated individuals within the BCRI have the authority to approve research proposals and to execute research agreements on behalf of the organization. All such research documents require Legal review and approval prior to execution.

The BCRI in cooperation with Corporate Privacy and Security ensures that appropriate required subject protection language is included in contracts. Any variations or revisions to standardly accepted terms in Confidentiality Agreements, Data Security and HIPAA/PHI related matters require the review and approval of the BMHCC Corporate Privacy Officer.

The BCRI, the HRPP, and Legal work in conjunction to confirm that the contract and the consent documents are consistent in terms of costs to subjects and who pays in case of injury.

The HRPP office coordinates efforts to ensure that all applicable individuals have filed appropriate conflict of interest (COI) disclosures to meet investigator COI policies.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of Baptist, a subcontract is executed between the Baptist entity and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval. The collaborating institution must also ensure that key personnel involved in human subject research are in compliance with their

institutional policy or NIH's policy on education in the protection of human research subjects and provide documentation of education of key personnel to the IRB staff.

1.11.8 Baptist Pharmacy

A pharmacist serves on the IRB, allowing the pharmacy to have complete information about all IRB approved research that takes place at Baptist entities and under its jurisdiction.

The pharmacist assures that information about all studies involving drugs used in research is shared with both the pharmacy staff as appropriate and that Baptist pharmacy is made aware of IRB approved research involving drugs.

The Baptist pharmacy or its affiliate pharmacies are responsible for storing, accounting for, dispensing, and compounding of most investigational drugs used in research, whether conducted inpatient or outpatients.

The manufacture/compounding of drug products not commercially available is coordinated by the Baptist pharmacies.
Waivers from use of the Baptist pharmacy for handling investigational drugs will be documented and considered on a case-by-case basis by both the IRB and the Baptist pharmacy, with required information regarding storage, accounting, dispensing etc. provided within the IRB application. The Research pharmacists and Pharmacy Service Line Administrator are available to provide guidance to investigators in relation to the management of the study drugs.

1.11.9 Relationship Among Components

The Assistant Director will facilitate and maintain a dialogue between the various compliance entities at the organization and will monitor compliance of existing programs, develop new or revised policies as changes in requirements occur and disseminate updated compliance information to the research community.

1.11.10 Study-Specific Coordination

In addition, prior to IRB approval and as applicable, the Investigator, or designee, must participate in a feasibility meeting in order to obtain and document the approval, support, or permission of other individuals and departments or entities impacted by the research as well as approval by any oversight committees and the entity's Chief Executive Officer or designee. For any studies requiring a feasibility meeting, a signed feasibility meeting form or letter or other evidence of support, collaboration, permission, or approval from the designated authority should be included in the Initial Submission Application to the IRB.

The application will be reviewed in the IRB office to ensure that all necessary approvals are included. Final IRB approval will not be given until all necessary letters are received.
The IRB may request review or consultation with any of the above listed or other organizational committees or components even when such review or consultation is not technically required by policy. Other committees and officials may not approve research involving human subjects to commence that has not been approved or has been disapproved by the IRB.

1.11.11 Collaborative Research Projects

In the conduct of cooperative research projects, Baptist acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When a cooperative agreement exists, the Baptist entity may choose to enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. See Section 6, External IRB Reliance.

1.11.12 State Laws

In addition to federal laws and regulations, human research activities conducted at Baptist entities must comply with all and any laws in the state in which the research is being conducted in accordance with 45 C.F.R. § 46. In general, when federal and state laws differ, the more restrictive law prevails.

The Principal Investigator has the responsibility for ensuring that a protocol complies with all regulations and statues governing human subjects' research and the HRPP should be responsible for documenting /stating which laws that directly impact research at Baptist entities, such as, age of consent, Legally Authorized Representatives (LAR) and who may serve as a LAR for surrounding states.

The departments of Legal Counsel and Compliance will serve as guides and references upon request. As specific issues arise, Legal and Compliance can discern the updated applicable law/statute/regulation upon request.

1.11.12.1 Policies by State (Age of Consent, Emancipated Minors, LARs)

Research at Baptist entities will be conducted in accordance with applicable laws of Tennessee, Mississippi, or Arkansas. [45 C.F.R. § 46]

Age of Consent/Age of Majority

Tennessee

Age of Majority means eighteen (18) years of age or older; except that when purchasing, consuming or possessing alcoholic beverages, wine or beer as those terms are defined in title 57, "Age of Majority" means twenty-one (21) years of age. [T.C.A. § 1-3-105]

Emancipated Minor Defined by T.C.A. §33-8-104

a. Marriage

b. Court Order

c. In any other way the person is recognized by Tennessee law to have all the rights and responsibilities of adults.

Mississippi

According to Mississippi State Law, Minors are persons under the age of twenty-one (21) years. The general rule is that a person may consent for his or her own medical care at the age of

eighteen (18) years. The statutes do not specifically allow a person aged eighteen to twenty (18-20) years to consent to research; and therefore, they should be considered as minors unless circumstances exist to confer majority status on the minor. Certain statutes and case law provide minors with majority status in some circumstances (e.g. emancipated minor, mature minor, or minor seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion). Miss. Code Ann. § 41-41-17, states that a parent or legal guardian may consent to allow an un-emancipated minor to participate in research.

Emancipated Minor by Court Order or Marriage

Arkansas

In Arkansas, "children" includes all those who have not yet reached their 18th birthday and have not been legally emancipated. Emancipation may be obtained through judicial decree or based upon certain events such as marriage or military service. Marriage or military service does not automatically emancipate an individual, and investigators should seek guidance if the issue arises.

Legally Authorized Representative (LAR). The question of who may serve as an LAR is a matter of state law.

Tennessee

The hierarchical order of person who may serve as LAR in Tennessee is specified in T.C.A. § 68-11-1806 and is as follows: Conservator; guardian; patient's spouse, unless legally separated; the patient's adult child; the patient's parent; the patient's adult sibling; any other adult relative of the patient; or any other adult who has exhibited special care and concern for the patient, who is familiar with the patient's personal values, who is reasonably available, and who is willing to serve as LAR. No person who is the subject of a protective order or other court order that directs that person to avoid contact with the research subject shall be eligible to serve as the research subject's surrogate.

Mississippi

In accordance with Miss. Code Ann. § 41-41-211 regarding consent for treatment, when the primary physician determines that a patient lacks capacity to give consent the order of authority to provide consent on behalf of another adult or emancipated minor is as follows:

1. Health care agent
2. Court appointed guardian
3. The spouse, unless legally separated
4. An adult child
5. A parent
6. An adult brother or sister
7. An adult who has exhibited special care and concern for the patient, who is familiar with the patient's personal values, and who is reasonably available

Arkansas

In Arkansas [Arkansas Code § 20-6-105], in addition to other persons as may be authorized and empowered, the legally authorized representative for another person, for purposes of providing

consent for research involving surgical or medical treatments or procedures not prohibited by law, will be identified by the supervising healthcare provider in descending order:

1. Supervising healthcare provider
2. Court appointed guardian
3. The principal's spouse, unless legally separated
4. The principal's adult child
5. The principal's parent
6. The principal's adult sibling
7. Any other adult relative of the principal
8. Any other adult person, who exhibited special care and concern for principal, who is familiar with the principal's personal values, who is reasonably available, and who is willing to serve. A person who is the subject of a protective order or other court order that directs that person to avoid contact with the principal is not eligible to serve as the principal's surrogate.

Wards of the State (foster children) [45 C.F.R. § 46.409]

Research involving children who are wards is generally not conducted at Baptist. See Section 15, Vulnerable Subjects.

Other Jurisdictions

Baptist investigators wishing to conduct research in a jurisdiction other than Tennessee, Mississippi, or Arkansas must provide assurance that the research will conform to the laws of that jurisdiction.

2 Quality Assurance

The Baptist HRPP performs Quality Assurance and Improvement activities for the purposes of monitoring the safety of ongoing studies and measuring and improving human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable federal, state, and local laws.

2.1 External Monitoring, Audit, and Inspection Reports

All reports from external monitors, auditors, or inspectors must be submitted by investigators to the IRB for review: Routine study monitoring reports that do not identify any study deviations may be submitted at the time of annual review. Audit, inspection reports, and study monitoring reports that identify study deviations must be submitted to the IRB upon receipt. The Assistant Director of the Baptist HRPP, IRB Chair, IRB Vice-Chair, or designee will review such reports in order to monitor for issues that may impact the rights or welfare of human subjects and for issues that could impact the rights or welfare of human subjects and for issues indicative of serious or continuing non-compliance (See Section 31, Reportable Event Research Non-Compliance). If such issues are identified, the report will be forwarded to the convened IRB to determine what additional actions are necessary.

When Baptist is engaged in research reviewed by an external IRB, all reports from audits or inspections must be submitted to the HRPP for review. The HRPP may require corrective and preventative actions (CAPA), a follow up review, or other actions as needed to ensure the protection of human subjects and to support compliance.

2.2 Investigator Compliance Reviews

The Assistant Director or designee is responsible for conducting post- approval directed ("for cause") audits and periodic (not "for cause") compliance reviews of investigator research. These may be performed internally, or requested of Corporate Audit, Corporate Compliance, or an outside consulting firm, as deemed appropriate. Additionally, the IRB may appoint a subcommittee for the purpose of conducting a for-cause or not for- cause compliance review of one or more research plans under its jurisdiction. The subcommittee may be composed of IRB members and staff from within, or individuals from and outside of the organization.

Compliance reviews are conducted to assess investigator compliance with federal, state, and local law, and Baptist HRPP policies to identify areas for improvement, and to provide recommendations based on existing policies and procedures. The results of compliance reviews will be reported to the Institutional Official, Assistant Director, the IRB, the investigator, and other Baptist leadership as appropriate. Any non-compliance will be handled according to the non-compliance policy, S.HRPP.1216 Reportable Event Research Non-Compliance.

If it is identified that subjects in a research project have been exposed to unexpected serious harm, the person(s) conducting the review will promptly report such findings to the Institutional Official, Assistant Director and the IRB Chair for immediate action.

If issues are identified that indicate possible misconduct in research, the procedures in the Research Misconduct Policy will be initiated.

Compliance reviews will be performed within the agreed-upon scope and may include, but are not limited to:

- Requesting progress reports from investigators
- Examining investigator-held research records and records held by pharmacy or other ancillary services
- Reviewing source documentation
- Reviewing the recruitment process and materials
- Reviewing consent materials and the documentation of consent
- Observing the consent process and other research activities
- Verifying HIPAA authorization
- Interviewing investigators and research staff
- Interviewing research subjects
- Reviewing projects to verify, from sources other than the investigator, that no unapproved changes have occurred since previous review
- Conducting other monitoring or auditing activities as deemed appropriate by the HRPP or IRB.

Results of the reviews will be documented using a checklist.

2.3 IRB Compliance Reviews

The Assistant Director will periodically review the activities of the IRB to assess compliance with regulatory requirements and to identify areas for improvement; this will include a review of IRB records at least annually. This may be performed internally, or requested of Corporate Audit, Corporate Compliance, or an outside consulting firm, as deemed appropriate. Review activities may include, but are not limited to:

1. Review of the IRB minutes to assure that quorum was met and maintained;

2. Review of the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review will include assessing the documentation surrounding the discussion for protections of vulnerable populations as well as risk/benefit ratio and consent issues that are included in the criteria for approval;

3. Review of IRB documentation, including IRB minutes, to assess whether privacy provisions, according to HIPAA, have been adequately reviewed, discussed and documented;

4. Evaluating the continuing review discussions to assure they are substantive and meaningful and that no lapse has occurred since the previous IRB review;
5. Reviewing IRB files to assure retention of appropriate documentation and consistent organization of the IRB file according to current policies and procedures;
6. Reviewing the IRB database to assure all required fields are completed accurately;
7. Verifying IRB approvals for collaborating institutions or external performance sites;
8. Reviewing the appropriate metrics (for example, time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process;
9. Reviewing the workload of IRB staff to evaluate appropriate staffing level; and
10. Other monitoring or auditing activities deemed appropriate.

The Assistant Director will review the results of IRB compliance reviews with the IRB and the Institutional Official. If any deficiencies are noted in the review, a corrective action plan will be developed by the Assistant Director and approved by the Institutional Official, Corporate Compliance, and Corporate Audit. The Assistant Director will have responsibility for implementing the corrective action plan.

2.4 HRPP Quality Assessment and Improvement

Annually, a meeting is held by the Assistant Director, in collaboration with Corporate Audit, in which the quality improvement plan is put into place, to be carried out by an individual or committee named by the Assistant Director that assesses compliance and achievement of targeted levels of quality, efficiency, and effectiveness of the HRPP (e.g., continuous investigator training; use of IRB-approved consent forms, turn-around time of exemption determinations, etc.). The plan will, at a minimum, contain the following:

- The goals of the plan with respect to achieving and maintaining compliance
    - At least one objective to achieve or maintain compliance
    - At least one measure of compliance
    - The methods to assess compliance and make improvements
- The goals of the plan with respect to achieving targeted levels of quality, efficiency, and effectiveness
    - At least one objective of quality, efficiency, or effectiveness
    - At least one measure of quality, efficiency, or effectiveness
    - The methods to assess quality, efficiency, or effectiveness and make improvements.

The Assistant Director is responsible for tracking internal metrics that are informative in considering IRB and Investigator efficiency such as the amount of time from receipt of a submission through pre-review, assignment to the IRB, and final approval and the amount of time it takes investigators to develop and submit responses to pre-review and IRB requirements. Metrics reports will be provided to the Assistant Director and IRB Chair twice per year.

Each year in December, the Assistant Director, in collaboration with the IRB Chair and IRB Coordinators, will develop a Performance Workplan that defines the Quality Improvement goals for the following year. The Workplan will address compliance with the HRPP in the areas of IRB operations, regulatory operations, and research operations, as well as addressing the quality, efficiency and effectiveness of the HRPP.

3 Education and Training

Recognizing that a vital component of a comprehensive human research protection program is an education program, Baptist is committed to providing training and an on-going educational process for IRB members and the staff of the IRB and HRPP Office, related to ethical concerns and regulatory and organizational requirements for the protection of human subjects.

3.1 New IRB Member Orientation and Education

3.1.1 Initial Education

New IRB members, including alternate members, will meet with the Assistant Director of the Baptist HRPP or designee for an informal orientation session. At the session, the federal regulations will be reviewed and an orientation to IRB processes will be given. New members are required to complete the initial education requirements for IRB members before becoming an active voting member. The requirements include review and completion of the following:

- Collaborative Institutional Training Initiative (CITI) courses IRB Member Basic and Biomedical Research Basic (https://www.baptistonline.org/services/clinical-trials-research/hrrp-and-irb)
- The National Institutes of Health Financial Conflict of Interest Tutorial
- Baptist Memorial Health Care Corporation financial conflict of interest (FCOI) disclosure form
- IRB Member Biographical Sheet
- IRB Member Agreement
- IRB Member Code of Conduct
- Tools used by IRB reviewers (checklists, etc.)
- Links to Federal Regulations and the Belmont Report
- HRPP Operations Policy, Procedure, and Guideline Manual
- Attend at least two (2) IRB meetings

3.1.2 Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB.

In addition to initial education requirements, IRB members and staff and the Assistant Director must also satisfy continuing education requirements on an annual basis. The Baptist HRPP uses the following activities as a means for offering continuing education to IRB members, HRPP and IRB Assistant Director and IRB staff:

- In-service training at IRB meetings;
- Monthly Research Roundtables
- Training workshops;
- Copies of appropriate publications;
- Identification and dissemination by the Assistant Director or designee of new information that might affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings.

IRB members and staff and the Assistant Director are also required to complete the IRB Member and Biomedical Research Refresher courses through the CITI portal every 3 years as part of the Baptist IRB continuing education requirements.

The activities for continuing education vary on a yearly basis depending on operating budget and areas of need, as determined by the Assistant Director. The Assistant Director or designee determines which continuing education activities are mandatory for IRB members and staff in a given year. The IRB Coordinator tracks whether each individual has satisfied the requirements. IRB members who have not fulfilled their continuing education requirements will not be assigned as primary or secondary reviewer until they are fulfilled. Continuing failure to complete training may result in the individual being removed or not renewed as an IRB member. Fulfillment of training requirements is included as part of the evaluation of the performance of IRB members/alternates.

Members and staff who are unable to attend education sessions will be provided with the opportunity to make up any training that they missed. If a make-up session is not possible (e.g., a webinar or conference), then an equivalent educational opportunity will be offered at the discretion of the Assistant Director.
The Institutional Official (IO) will provide support to send as many members of the IRB as possible to attend the annual PRIM&R conference, regional OHRP conferences or other conferences/symposia on human research protections.

3.2 Training / Ongoing Education of Investigators and Research Team

3.2.1 Initial Education

Investigators, key personnel, and other members of the research team must complete the Baptist required human subject protection courses through the CITI portal (https://www.baptistonline.org/services/clinical-trials-research/hrrp-and-irb). Required courses are based upon the type of research being conducted. Courses include the

Basic/Refresher Course in either Biomedical, Social/Behavioral or Data/Specimen Only Research, Good Clinical Practice (for biomedical researchers), and either Biomedical or Social/Behavioral Responsible Conduct of Research. There are separate courses for students enrolled at the Baptist University of Health Sciences.

A certificate of completion is given for each course successfully completed with a passing score of 80% and remains in effect for three (3) years. Evidence of current training for each member of the research team must be included in every initial and continuing review application submitted to the IRB. Submissions from investigators who have not completed the education requirements will not be approved.

While research plans and applications for continuing review will be accepted and reviewed if the investigator holds a current certification of training, final approval will not be granted until all co-investigators and members of the research team have completed applicable education requirements.
In addition to human subject protection and conflict of interest education, principal investigators and all research staff engaged in research must provide documented acknowledgement and awareness of Baptist-specific policies outlined in the Baptist HRPP Operations Policy, Procedure and Guideline Manual.

3.2.2 Waiver of Education

Individuals must migrate courses taken through the CITI portal at other institutions by affiliating with Baptist Memorial Health Care (TN, MS, AR) on the CITI website. Additional courses may need to be completed if the minimum coursework requirements are not met after migration.

3.2.3 Continuing Education and Recertification

Investigators, key personnel, and other members of the research team must meet the Baptist continuing education requirement every three (3) years after initial certification as long as they are involved in human research. There is no exception to this requirement. Affected individuals must complete appropriate refresher modules through the CITI portal. Other training may be acceptable if approved by the Assistant Director.

Individuals must submit to the IRB office evidence of continuing education prior to the expiration of their training certification. New research plans and applications for continuing review will not be accepted from investigators who have not submitted satisfactory evidence of continuing education.

Investigators who are also IRB Chair, IRB members, or IRB Office staff should satisfy the training requirements for IRB members and staff described above.

4 "Human Subjects" and "Research" Determinations

4.1 Responsibility and Requirements

The responsibility for initial determination whether an activity constitutes human subject research rests with the investigator. The investigator should make this determination based on the definitions of "human subject", "research" and "clinical investigation" as described in Section 1.9. Because determination can sometimes be complex, and investigators will be held responsible if the determination is not correct, investigators must obtain confirmation that an activity does not constitute human subject research from the IRB Office by submitting a Human Subject Research Determination form through IRB Manager.

When research involves the use of coded private information or specimens, and the investigator makes an initial determination that the research does not include "human subjects", the investigator must obtain confirmation from the IRB as described above. Under the Common Rule, information is considered identifiable, and thus involving human subjects, when the identity of the subject is or may readily be ascertained by the investigator or associated with the information. It should be noted that this definition differs significantly from de-identified in accordance with HIPAA standards. FDA regulations do not incorporate the concept of "identifiability" in the evaluation of whether an activity is a clinical investigation (or research) subject to FDA regulations. For example, the use of de-identified human specimens to evaluate the safety or effectiveness of a diagnostic device is considered human subjects research subject to FDA regulations.

Human Subjects Research Determinations must be submitted, and determined, prospectively (i.e., before the proposed activity or research begins). Conducting human subjects research without IRB approval or exemption is noncompliance and will be managed as described in Section 18.

4.2 Examples of activities that are not considered research:

1. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

3. Collection and analysis of information, biospecimens, or records by or for a criminal

justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

5 Exempt Determinations

5.1 Exempt Studies

All research using human subjects must be approved by the Baptist IRB. Although certain categories of human subject research are exempt from IRB oversight, at Baptist, the determination of exempt status must be made by the IRB Staff, or, if limited IRB review is required to meet a particular exemption (see below), the IRB Chair or designee will make the determination. Baptist may also choose to accept an exempt determination made by an external IRB, on a case by case basis.

Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research. Reviewers must not have any apparent conflict of interest. Identification of individuals designated to conduct exempt determinations will be made in writing.
Unless otherwise required by law or by Federal department or agency heads, exempt studies are exempt from the Common Rule [45 CFR 46] (i.e., IRB approval and full research consent are not required) other than as specified within the regulations (e.g., the conditions that permit exemption, and when limited IRB review is required). Exempt research is not exempt from ethical considerations, such as honoring the principles described in the Belmont Report. The individual(s) making the determination of exemption will determine whether to require additional protections for subjects in keeping with ethical principles (e.g., requiring disclosure/consent, etc.).

5.2 Limitations on Exemptions

5.2.1 Children:

Exemption #2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed.

Exemption #2(iii), where identifiable information is obtained and the IRB conducts a limited IRB review, is NOT applicable to research in children.

Exemption #3 does NOT apply to research involving children. [45 CFR 46.104(b)(3)]

5.2.3 Prisoners:

Exemptions do not apply except for research aimed at involving a broader subject population that only incidentally includes prisoners. [45 CFR 46.104(b)(2)]

5.3 Categories of Exempt Research (45 CFR 46.104)

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the

comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), if at least one of the following criteria is met:

    i. Information obtained is recorded in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

    ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, educational advancement or reputation; or

    iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7): When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

3. (i) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

    A. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

    B. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

    C. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by [45 CFR 46.111(a)(7)] When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

    (ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such

criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

1. Secondary research for which consent is not required: Secondary research uses of (existing or prospectively collected) identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

    i. The identifiable private information or identifiable biospecimens are publicly available;
    ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
    iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
    iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

2. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by

Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

i. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

3. Taste and food quality evaluation and consumer acceptance studies:

i. If wholesome foods without additives are consumed, or
ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

5.4 FDA Exemptions:

The following categories of clinical investigations are exempt from the requirements for prior IRB review and approval:

i. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article is subject to IRB review. [21 CFR 56.104(c)]
ii. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR 56.104(d)]

5.5 Investigator Procedures for Exemption Determination

In order to obtain an exemption determination, investigators must submit the following to the IRB:

a. Using the IRB Manager X-Form, a completed application for exempt status;

b. All recruitment materials (e.g., letter of invitation, recruitment script, flyer);

c. Consent form/disclosure/information sheet (when appropriate);

d. All surveys, questionnaires, instruments, etc., if applicable;

e. Letter(s) of permission from each non-Baptist site of performance, if applicable;

f. If sponsored/funded, one copy of the grant application(s) and/or contract.

5.6 IRB Procedures for Exemption Determination

The IRB Staff and/or IRB Chair or designee reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The reviewer's determination is documented on the Exemption Determination Checklist and is kept with the study file. If the request does not appear to meet the definition of human subject research, the reviewer evaluates the proposal as described above.

When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the limited review may be conducted using expedited review procedures by the IRB Chair or an experienced Chair-designated member of the IRB. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval.

Actions of disapproval may only be made by the convened IRB. [45 CFR 46.109(a), 45 CFR 46.110]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within five (5) business days). [45 CFR 46.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case it shall document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [45 CFR 46.109(f)(ii), 45 CFR 46.115(a)(3)]

The individual making the determination of exemption will determine whether to require additional protections for subjects in keeping with the guidelines of the Belmont Report.

If there are interactions with participants, the reviewer should determine whether there should be a process for prospective agreement that will disclose such information as:

i. That the activity involves research.

ii. A description of the procedures.

iii. That participation is voluntary.

iv. Name and contact information for the researcher

The reviewer indicates in the reviewer checklist whether the request for exemption was approved, the rationale for the determination and category/s under which it was permitted. The exempt application, review form, and determination letter are recorded and maintained in the same manner and for the same length of time as other IRB review documentation.

Once the exemption review is completed, IRB staff will send written notification of the results of the review to the investigator.

Exempt determinations are for a 12 month period. Just prior to the 12 month point, an annual check-in form that requests verification of research activity and study personnel must be completed. If the research is no longer being conducted, at the time of the annual check-in the investigator may choose to close the study. This process will allow the investigator and the organization the opportunity to review and update the research activity and determine whether or not it still qualifies for exemption. Similarly, investigators should report to any proposed modifications to the research during the course of the exempt study for a determination of whether or not the modified activity still qualifies for exemption.

6 External IRB Reliance

When engaged in multi-site research, research involving external collaborators, or research that is otherwise under the jurisdiction of more than one IRB, Baptist acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. Baptist may choose to review the research in its entirety, only those components of the research Baptist is engaged in, rely on the review of another qualified IRB, or make other arrangements for avoiding duplication of effort. When Baptist is the prime awardee on an HHS grant, it will ensure that at least one IRB reviews the research in its entirety.

When relying upon another IRB or when serving as the reviewing IRB for an outside organization or external investigator, a formal relationship must be established between Baptist and the outside organization or investigator through an IRB Reliance, Agreement, Investigator Agreement, a Memorandum of Understanding, or other such written agreement. The written agreement must be executed before Baptist will accept any human research proposals from the outside organization or investigator or rely on the review of an external IRB.

IRB reliance agreements establish the authorities, roles, and responsibilities of the reviewing IRB and the relying organization. The procedures for reliance, including those for communication, information-sharing, and reports, may be outlined in the reliance agreement, in SOPs, or other written materials. The HRPP office staff utilizes a checklist to ensure that reliance agreements and any accompanying materials address all requirements and are consistent with Baptist's standards. To support compliance, Baptist will make every effort to ensure as much consistency as possible across reliance agreements.

With the exception of NCI CIRB, requests for Baptist to either rely upon an external IRB or to serve as the IRB of record for an external organization or investigator requires prior approval through the IRB/HRPP Office. These requests should be submitted as early as possible in the grant/contract process by following the procedures outlined in this policy for requests to use an external IRB or submission of HRPP 614 Supplement L Collaborative Research for use of Baptist IRB in multi-site studies.

Baptist has signed the SMART IRB joinder agreement. When the organizations participating in the research are signatories to the joinder agreement, IRB reliance may be requested and documented utilizing the SMART IRB online reliance platform. In collaboration with the other participating organizations, Baptist will determine on a study-by-study basis whether the SMART IRB SOPs or alternative procedures will be utilized to implement the reliance.

Baptist has standing agreements in place to engage the services of external IRBs for the review of specific categories of research including:

1. NCI's Adult CIRB for NCI research involving adult
2. Vanderbilt Ingram Cancer Center
3. WCG IRB for biosafety research

Research involving only data review must by reviewed by the Baptist IRB and are not eligible for review by external IRBs.
Regardless of which IRB is designated to review a research project, Baptist is responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, approval, and oversight by Baptist and must adhere to all applicable policies, procedures, and requirements, including those of the Baptist HRPP.

6.1 Baptist Serving as Reviewing IRB

Generally, Baptist IRB does not serve as the IRB of record for an external organization unless Baptist is also engaged in the research or has a master agreement in place with the external organization. The Assistant Director, the IRB Chair or designee, and the Corporate Legal Services Department evaluate the following factors, and others as appropriate, when considering a request for the Baptist IRB to serve as the IRB of record for a particular study or studies:

4. The terms of the external organization's FWA;
5. Prior experience with the organization and investigators;
6. The accreditation status of the external organization's HRPP;
7. The compliance history of the organization and investigators (e.g., outcomes of prior audits or inspections, corrective actions);
8. The research activities conducted by or at the external organization;
9. The willingness of the external organization to accept Baptist's reliance terms and procedures;
10. The ability of the organizations to collaboratively provide meaningful oversight of the proposed research, taking into account factors such as:

    a. The risks and procedures of the research;
    b. The resources available at each organization and ability to accommodate or collaborate with each other in observing the consent process, performing compliance reviews, investigations of potential noncompliance, and similar matters;
    c. The expertise and experience of the Baptist IRB with the proposed research, subject population, and applicable regulations;
    d. The familiarity of the Baptist IRB with the relevant local context considerations of the external organization; and/or
    e. The willingness or ability of the external organization to provide information and respond to questions regarding investigator qualifications, conflicts of interest, organizational requirements, local context, and other matters that may inform the IRB review.

When the Baptist IRB serves as the reviewing IRB for another organization, the requirements and procedures outlined throughout the HRPP Baptist policies apply unless an alternative procedure has been agreed to in the reliance agreement or outlined in a companion document.

For example, alternative procedures may be used for any of the following:

1. Management and documentation of scientific review, other ancillary reviews, and institutional permissions for research;
2. Training requirements and verification of qualifications and credentials for external investigators and staff;
3. For-cause and not-for-cause compliance reviews;
4. The disclosure and management of conflicts of interest. In all cases, any COIs and CMPs identified and developed by the relying organization will be communicated to the reviewing IRB. The reviewing IRB will determine the acceptability of the plan in accordance with their policies and procedures.
5. Review and management of matters such as site-specific consent language, HIPAA (e.g., authorizations, waivers, alterations), noncompliance, unanticipated problems, and federal reports;
6. *Optional:* Ensuring concordance between any applicable grant and the IRB application/protocol.
7. Procedures for and type of IRB review (e.g., expedited, convened) of additional sites after the research protocol is IRB-approved;
8. Procedures for submission and review of interim reports and continuing review materials; and/or
9. The communication of IRB determinations and other information to external investigators and organizations.

6.2 External IRB Review of Baptist Research

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to 45 CFR 46.104(d)(2)(iii) or (d)(3)(i)(C) that Baptist is engaged in must be reviewed and approved by the Baptist IRB or an external IRB that Baptist has agreed to rely upon prior to the initiation of the research.

Baptist may choose to enter into an agreement to rely upon other external IRBs, most commonly when required as a condition of a grant or contract. Investigators should submit reliance approval requests as early in the grant/contract process as possible by emailing the 'Request to Use and External IRB Form' to the HRPP/IRB Office.

The Assistant Director of the HRPP, the IRB Chair or designee, and the Corporate Legal Services Department evaluate the following factors, and others as appropriate, when considering a request to rely up

on an external IRB:

1. The accreditation status of the proposed IRB.
2. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective actions);

3. Prior experience with the IRB;
4. The federal IRB registration and organizational FWA, as applicable;
5. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
6. The research activities that will be conducted at or by Baptist;
7. The risks and complexities of the proposed research;
8. The proposed reliance terms and procedures including the procedures for collaborative management of matters such as conflicts of interest, noncompliance, unanticipated problems, and federal reports;
9. The plan for review and allowance of the incorporation of site-specific consent language;
10. The plan for incorporation of other relevant local requirements or context information in the review process;
11. Assessment of any prior non-compliance or other issues by the Baptist investigator; and
12. Involvement of special populations, e.g., minors, adults unable to consent for themselves

When reliance on a non-accredited IRB is proposed, the evaluation may also take into consideration one or more of the following based upon the risks of the research, the research activities that Baptist will be involved in, and Baptist's familiarity with the IRB:

1. When the research is minimal risk (or the activities that Baptist is involved with are minimal risk), a statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization's FWA;
2. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance using the FDA's self-evaluation checklist or AAHRPP's self-evaluation instrument;
3. The willingness of the external IRB to accommodate requests for relevant minutes and other records of the proposed study and/or to copy Baptist's HRPP office on correspondence such as determination letters and notices of suspensions or terminations of IRB approval;
4. The willingness of the external IRB to accommodate a request for someone from the relying organization to serve as a consultant to the IRB or to observe the review of the proposed study; and/or
5. An assessment of the external IRB's policies and procedures.

The external IRBs that serve as the IRB of record for Baptist research have the same authority as the Baptist IRB and all determinations and requirements of the external IRBs are equally binding. Investigators must be familiar with and comply with the external IRB's policies and

procedures and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs).

6.2.1 Baptist-required Approval for Use of External IRBs

Investigators must obtain approval from Baptist for use of an external IRB. Prior to submitting the application package to the external IRB, the investigator must provide the following information/documents to the HRPP Office:

1. Baptist IRB Application: Request to Use External IRB;
2. Operational Feasibility Report: This is necessary for record-keeping and to assess the impact of the proposed activity on Baptist's patients, services and facilities for all inpatient studies;
3. Study Personnel: This is necessary for record-keeping and to ensure that any applicable training/credentialing and COI requirements have been satisfied;
4. Study Information (Sponsor, identifiers, IDE/IND No. (if applicable) and Study location(s);
5. Confirmation that the sponsor will accept direct invoicing from the external IRB and allow direct payments to external IRB;
6. Sponsor Protocol/research plan document;
7. Baptist template consent document reviewed by Baptist Legal;
8. Authorization Agreement between Baptist and the External IRB of record

If using an external IRB, the investigator or sponsor completes any of the IRB's required materials.

HRPP office staff will review the submitted information and verify that CITI training, COI review, and any other applicable approvals or requirements (e.g., operational feasibility etc.) have been completed, and determine the need for relaying local context information (e.g., specific Baptist policies concerning minors or adults without capacity to consent etc.) to the reviewing IRB in accordance with the reliance agreement.

Once the above are reviewed and approved by the Assistant Director or designee, the investigator will be notified that they may move forward with their submission to the external IRB by receipt of the signed Institutional Jurisdiction Waiver Form/IRB reliance Agreement from the Baptist HRPP Office.

When applicable, and when the external IRB is not responsible for reviews of requests for waivers or alterations of HIPAA authorization (e.g., studies reviewed by the NCI CIRB), the HRPP staff will forward requests for waiver or alteration of HIPAA authorization and any relevant materials to the internal IRB Chair or a designated expedited reviewer for review. The HRPP office staff will notify the investigators by email once the proposed research has been approved for submission to the external IRB.

Once approved by the external IRB, investigators must email a copy of the approval notice

and any approved consent document(s) to the HRPP Office. If the protocol was modified during the external IRB review process, the approved version of the protocol should be provided as well.

6.2.2 Post-approval Requirements for Studies Relying on an External IRB

Baptist retains certain on-site responsibilities for all studies reviewed by any external IRB, including sharing reports of site monitoring activities which have any findings that potentially impact human subject protections with the external IRB.

The Baptist investigator must:

1. Copy the IRB Office on the initial, continuing, amendment, and study closure reviews and subsequent approvals. Alternatively, the Baptist IRB/HRPP may be copied on determination notifications that come directly from the external IRB and be granted access to study documents through the external IRB's electronic research management system is acceptable. Regardless of the method, the Baptist IRB must receive copies within ten (10) business days of receipt by the Principal Investigator or the study team.
2. Report local unanticipated problems, complaints, non-compliance, and sponsor audit, inspection, monitoring reports to the Baptist HRPP Office within five (5) business days of notification.
3. Submit requests for changes in study personnel to the Baptist IRB Office prior to permitting the personnel to assume any study responsibilities.

6.2.3 National Cancer Institute's Central IRB (NCI CIRB)

Requests by Baptist investigators to open a study that has been approved by the NCI CIRB are made by submitting the following materials to the Baptist HRPP Office:

1. Study Summary (ClinicalTrials.gov listing);
2. Key Personnel;
3. CIRB initial approval and continuing review;
4. The protocol/research plan version, investigator brochure(s), and model consent currently approved by the NCI CIRB;
5. The consent form;
6. Translations of the consent form for local use with accompanying certificates of translation.

6.3 National Institutes of Health Single IRB (sIRB) for Multi-Site Research

In June 2016, the National Institutes of Health (NIH) released a final policy requiring domestic awardees and domestic sites of NIH-funded multi-site research to use a single IRB (sIRB) for review of non-exempt human subject research unless there is justification for an exception. This policy is intended to streamline the IRB review process and reduce inefficiencies and redundancies while maintaining and enhancing subject protections. The policy does not apply to career development, research training, or fellowship awards, nor to sites that are not

conducting the same protocol as the other sites (e.g., sites providing statistical support or laboratory analysis only) or to foreign sites.

Exceptions to the policy are automatic when local IRB review is required by federal, tribal, or state law/regulation/policy and when the proposed research is the "child" of a grant that predates the requirement for sIRB review. Such exceptions and the basis (and information regarding the "parent" study, when applicable) should be cited in the proposed sIRB plan and, when the exception is based on law/regulation/policy, apply only to the site(s) to which the law/regulation/policy applies. Other exceptions will be considered when there is compelling justification. The site(s) and justification for why the site(s) cannot rely on the single IRB of record should be included in the proposed sIRB plan. The NIH will consider the exception request and inform the applicant of the outcome.

6.3.1 Selection and Designation of an sIRB

Baptist's investigators submitting applications for NIH-funded multi- site research must describe the sIRB plan in the funding proposal (grant application or contract proposal), and, if applicable, may request direct cost funding to cover additional costs related to the requirements of the NIH policy. The sIRB can be the IRB at one of the participating sites or an independent, fee-based IRB. When the sIRB is named in the proposal, the IRB must have agreed to take on this responsibility in advance. Requests for the Baptist's IRB to serve as the sIRB should be directed to the HRPP office. The Assistant Director will consult with others within the organization as needed and make a recommendation to the IO for consideration. Requests for Baptist to rely upon an external IRB as the sIRB should be submitted as early in the process as possible.

6.3.2 Reliance Agreements for sIRB Studies

A Reliance Agreement (or "Authorization Agreement") between the sIRB and the participating sites is required. The Reliance Agreement documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Reliance Agreements should describe the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval. When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing), the agreement or written procedures should indicate who is responsible for meeting the certification requirements. The agreement or written procedures should also specify points of contact and contact information for the sIRB and relying institution(s).

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

6.3.3 Responsibilities

The sIRB will be responsible for compliance with the regulatory requirements for IRBs specified in the federal regulations (i.e., 45 CFR 46 and other applicable regulations) and for any other responsibilities outlined in the reliance agreement and/or procedures. Participating sites (Relying institutions) are responsible for providing relevant local context information to the sIRB, ensuring that the research is conducted in accordance with applicable regulations and the determinations and requirements of the sIRB, and for other responsibilities, as outlined in the reliance agreement and/or procedures.

When an external IRB serves as the sIRB for a study in which Baptist is engaged, investigators must register the study with Baptist prior to submission to the external IRB following the procedures outlined in Section III(F) of this policy. Post-approval requirements are summarized above in Section 6.2.2.

Research reviewed by external IRBs remains subject to review, approval, and oversight by Baptist and must adhere to all applicable policies, procedures, and requirements, including those of the Baptist HRPP.

7 Research Previously Approved by Another IRB

When an investigator transfers human subjects research to Baptist that was previously approved by another IRB, the investigator must:

- Submit the research for review by the Baptist IRB or determination of exemption; or
- Submit a request for Baptist to rely upon the existing IRB of record (such requests must be approved by both organizations)

Research determined to be exempt at the previous institution will be reviewed according to the procedures in Section 5. All other research must be submitted as if it were undergoing initial review and will be reviewed under expedited review or by the convened IRB. Research activities under the auspices of Baptist cannot commence until all necessary approvals are in place including approval by the internal IRB or an IRB reliance agreement is executed (and the transferred activities are approved by the IRB of record).

For research transfers where stopping research interventions or procedures might harm subjects, the investigator can request permission from both organizations to continue the research under the oversight of the prior organization's IRB until final Baptist IRB approval is obtained.

8 HRPP/IRB Emergency Preparedness, Continuity and Recovery

Although relatively infrequent, emergencies and disasters of all types can occur and have a devastating effect on institutional operations that also affect research operations. In any emergency, there are both individual department and institutional responsibilities to ensure timely and efficient resumption of research activities after the emergency or disaster. Organizations should have a Business Continuity Plan (BCP) that encompasses the entire organization and a HRPP BCP should fit within the larger organizational BCP, but must be specific for how research operations will continue after, for example:

- A hurricane destroys infrastructure and communication and prevents access for an extended period
- Major flooding causes damage to research facilities
- A tornado causes structural damage to organizational and research buildings
- An earthquake that destroys infrastructure and disrupts communication
- A blizzard causes power loss and prevents access to research facilities
- A pandemic causes closure of the research facilities and impacts a large percentage of research staff for an extended period
- Organizational and/or HRPP electronic systems are compromised
- Some other event that causes long-term disruption of operations

To ensure that research participants are protected from research-related harms during an emergency or disaster, it is essential that the HRPP be able to function in its protective capacity throughout the disruption. For example, subjects in research may need to continue their investigational interventions (drug, device, behavioral) or receive an alternative intervention to assure their safety and well-being or research plans may require cessation of enrollment and/or changing to remote interactions or locations rather than having subjects come to the research site to complete research required activities (e.g., follow up exams, receipt of investigational products, etc.).
The Human Research Protection Program (HRPP) at [Organization] is committed to protecting the rights and welfare of research participants during both normal and emergency operations. The procedures described in this section are intended to assist in:

- maximizing the effectiveness of the HRPP's response to emergencies and disasters;
- ensuring HRPP operational continuity to the extent possible throughout the emergency or disaster; and
- protecting research subjects and efficiently recovering from disruptions from emergency situations.

8.1 Preparedness

The Assistant Director, in collaboration with the IRB Chair, is responsible for developing and maintaining the HRPP emergency preparedness, continuity and recovery plan. The overall plan is intended to cover a worse-case scenario, however, only the components of the plan that are required for the specific emergency will be implemented. The HRPP plan will coincide and coordinate with the existing Baptist Business Continuity Plans.

8.1.1 Key Contact List

Perhaps the most important component of a BCP is knowing who to contact during an emergency or disaster and how to contact them assuming communication disruptions. Therefore, the IRB Director will develop a list of key HRPP emergency contacts and their contact information to aid in communication and coordination during an emergency, as well as the emergency contact list for the organization. These lists will include cell phone numbers assuming that the contacts may not be able to be on-site during the emergency. The list will include HRPP and IRB staff and the Institutional Official and may also include specific researchers and staff.

Organizational emergency contact lists may include, but are not limited to:

- Information technology staff that support the HRPP/IRB systems
- Facilities management and critical infrastructure support (power, water, heat, etc.)
- Organizational security
- Human resources and payroll
- Organizational leaders
- Federal agencies/funding sources

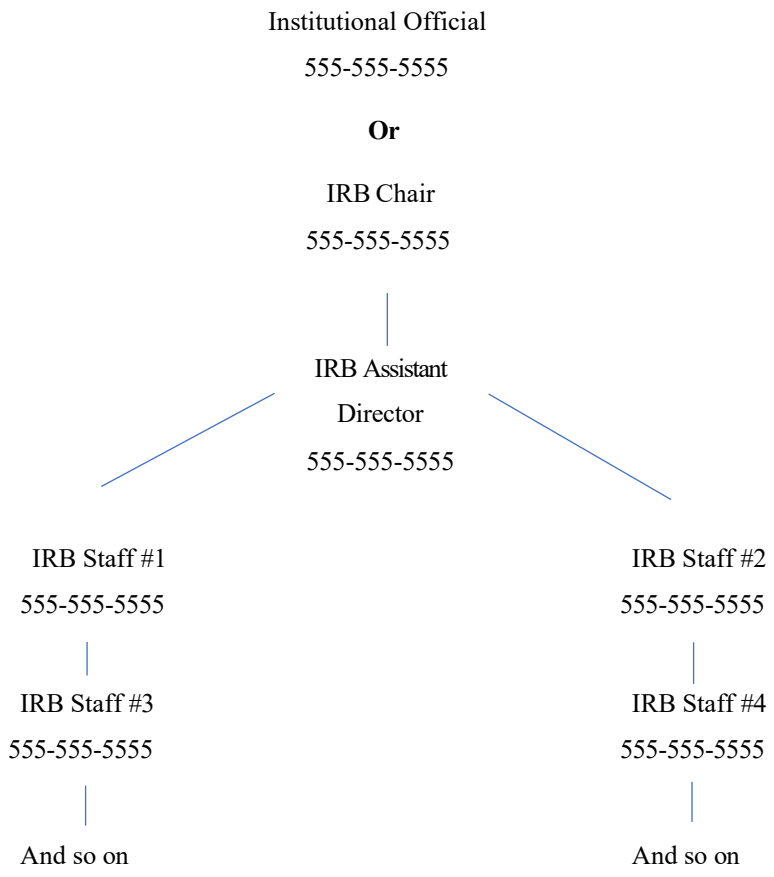
The IRB Director will keep a written copy of the list in a location that can be readily accessed assuming that normal internet and intranet services will be lost.

8.1.2 Establish an emergency communication plan, test it periodically and revise as necessary

Communication Methods

To ensure effective and timely communication during an emergency or disaster, the Assistant Director will develop a "call tree" that is a hierarchy or "tree" of people in which each person calls and forwards a message to the next person down the tree. For example, the Institutional Official or IRB Chair are listed at the top of the call tree and calls the person below them on the tree, and so on. The "tree" can be branched for efficiency and expediency to reduce the number of calls any single person is required to make and assist in getting everyone notified as quickly as possible. If a person on the list does not answer, the caller skips to the next person on the tree to ensure that as many people as possible are contacted. The last person(s) on the call tree contacts the first person on the call tree to confirm that the calls/messages went through the entire call tree. This ensures that all individuals on the tree receive the communication.

For example:



Assuming that cell phone coverage is intact, communications will be conducted using cell phone service and the call tree. Anticipating that the volume of cell phone calls will increase during an emergency, for less emergent calls, the plan may also include specified call times to attempt to communicate at times where call volumes are expected to be lower (e.g., early or late in the day).

Assuming that cell phone coverage and internet service will be disrupted, the plan will also include other methods of making contact with HRPP/IRB and key organizational staff. These methods might include meeting in-person at off-site locations at specified times. If possible, procedures for utilizing local radio and television services to communicate messages to institutional personnel should be established. If this can be established, the BCP should provide information on the stations that should be monitored.

The BCP should also include methods for communicating the procedures and/or adjustment to procedures that will be implemented during an emergency or disaster.

Periodic Testing

The Assistant Director is responsible for assuring that the call "tree" is constantly up to date. Individuals can be added or removed as necessary to represent the most current staffing. The IRB Director should test the call tree at least annually to assure that all individuals are available at the numbers listed. In order to assure a more realistic assessment of the call tree,

tests should not be announced. All individuals on the tree should carry or have immediately available to them, a copy of tree in the event a test is initiated, or an actual emergency occurs.

8.2 BCP plan input

The IRB Director, in collaboration with the IRB Chair, will ensure that input from all HRPP components and applicable organizational units is sought, considered and discussed. Facilities Management should be involved to describe when a building or office is not safe or operational, who will make that determination, how to contact that person(s), if/when relocation of HRPP operations will be required and how the relocation will be communicated and accomplished. This part of the plan should describe who is responsible for and how paper-based files will be relocated, stored, secured and maintained, when necessary.

Information Technology (IT) should provide a description of the organizational priorities that will impact the level of support that can be expected for HRPP electronic systems. Other organizational offices should contribute if they have the potential to affect HRPP operations. A critical factor in developing the HRPP BCP will be having individuals who are responsible for the organizational BCP be part of the HRPP planning process to assure that the organizational and HRPP BCPs can be carried out without significantly impacting either plan.

8.3 Management of HRPP operations during emergencies.

It is likely that normal operations will not be possible during an emergency and adjustments to IRB submissions, COI disclosures, sponsored program activities, etc. will need to be made. The HRPP BCP should inform stakeholders (staff, organizational officials, researchers, etc.) as to what the adjustments will or might be, how emergency operations will be conducted during an emergency or disaster and the potential impact of implementing the BCP. As much as possible, the emergency or disaster should be "triaged" to determine the types and extent of adjustments that must be made. There can be many possibilities. For example:

- In a severe emergency with significant infrastructure loss or disruption, suspension of new protocol submissions and/or review and execution of new contracts, except in extraordinary circumstances, will likely be required, however, continuing review and amendment requests, unanticipated problem reports and other time-sensitive reviews will have to be accepted and processed to assure that protection of research subjects is not interrupted. The HRPP BCP must describe:
    - How to contact the Institutional Official, IRB Chair and the IRB Director
    - How the time-sensitive submissions will be accomplished and processed
    - How results of IRB review will be communicated to researchers
    - Assuming disruption of electronic system operation, how records will be maintained for the duration of the emergency
- To be as efficient as possible, a new IRB, with the regulatory minimum number of members (5) and make-up (one non-scientist, one scientist, a physician for FDA-regulated studies, one non- affiliated) may need to be established to review the time-sensitive submissions, assure subject safety and well-being and prevent lapses in IRB approval. In this situation, applicable regulatory agencies should be notified, as soon as possible.

    - IRB meetings may be conducted face-to-face, by tele- or videoconference or by a combination or all three but may change from meeting-to-meeting due to loss or restoration of internet and phone service.

- For studies with investigational drugs or devices, arrangements will need to be made as to where the drugs or devices should be shipped (alternate pharmacy) and how investigational drugs will be stored (refrigeration available, locked area for controlled drugs, etc.) and segregated (separate location from non-investigational drugs) at the alternate location, how security at the new location will be assured, how the drugs will be dispensed to research subjects and other functions that assure FDA regulatory compliance relating to receipt, storage, dispensing and accountability are in place and appropriate.
- In the event of infrastructure destruction or loss of operational capability or in the interest of staff safety, IRB and other HRPP activities may need to be relocated to sites in other areas of the institutional facilities or remote from institutional facilities. Advance arrangements must be in place that ensures site availability so several contingent sites may need to be identified. The sites should have appropriate security, HVAC, electrical power, water, internet service (if possible) and be easily accessible, if in-person operations are required.
    - For paper-based systems, relocation must be to a secure location to ensure file integrity throughout the emergency or disaster. Appropriate utilities must be in place to control temperature and humidity.
    - The electronic IRB HRPP files at Baptist[Organization] are stored on a server used for day-to- day operations that is not at the organization's physical location (cloud service) and are backed up at least daily.
    - HRPP staff must have access to files. If some or all of the files are paper-based, in- person access must be granted to applicable staff. If the files are electronic, VPN access should be granted for applicable staff to allow access from home or another remote location.

8.4 Communication of the BCP prior to having to use it in an emergency or disaster

All HRPP components and applicable organization officials and departments should have access to a copy of the HRPP BCP. At least annually, the BCP should be reviewed to assure that all information in the plan is accurate and up to date. If necessary, the IRB Director, in collaboration with the IRB Chair, will make revisions to and update the BCP. After each review, a pdf copy of the BCP will be electronically available to all HRPP components, applicable organizational officials and those responsible for carrying out the organization's BCP in the event of an emergency or disaster.

8.5 Periodic verification of the BCP

It is essential that the BCP plan is accurate and can actually be implemented in an emergency or disaster. To verify that the BCP will be able to support HRPP operations, the IRB Director should periodically:

- Test the communication system(s) to assure that those that need to be contacted can be contacted;

- Conduct on-site audits of locations to which operations may be relocated;
- Verify how servers and their back-up procedures respond to power outages and other types of disruption that might occur;
- Evaluate access to buildings, paper-based and electronic files and relocation sites that may be required during an emergency or disaster.

8.6 Training of HRPP staff on the BCP

To assure that all HRPP staff are aware of might be required of them during an emergency or disaster, situational training will be provided and may be required for specific individuals. Training will include how normal operations could be affected, the adjustments that may have to be made and specifically how operations may have to be carried out during an emergency or disaster. The training will be developed and conducted by the Assistant Director in collaboration with the IRB Chair, as needed.

8.7 Continuity

To ensure continuity of operations as much as possible, the plan will be followed to the extent required to ensure continued HRPP operations and ensure that subjects remain protected. Modifications to the BCP and/or implementation of temporary HRPP/IRB Standard Operating Procedures may be required as emerging conditions develop.

IRB continuing reviews, amendments and unanticipated problem reports will be processed and reviewed so that approval for research studies does not lapse and that subject protections remain in place. Reviews may be conducted through an expedited process, when applicable, or through review at a convened meeting of the IRB. Depending on the specific situation, a newly established IRB with the minimum required membership may review the submissions for the duration of the emergency or disaster.
Other HRPP components will likely adjust their operational procedures, and these should be described in the BCP.

8.8 Recovery

Upon recovery from the emergency situation, resumption of normal operational SOPs will proceed at the fastest possible rate, but complete recovery will be dependent on the extent of procedural changes that were made for the emergency. If the HRPP/IRB offices and files were relocated, arrangements will need to be made to return staff and files to the on-site location. The BCP should include important steps to take, required resources, and key contacts needed to complete the task. An effective recovery strategy and recovery tasks should be easily understood by all involved with the recovery.

9 Institutional Review Board

Baptist has established an Institutional Review Board (IRB) to ensure the protection of human subjects in research it engages in.

9.1 Authority of the IRB

The authority of the IRB derives from federal regulations (45 CFR Part 46 and 21 CFR Parts 50, 56, 312, 812). Additional authority, as specified in the various policies and procedures for the Baptist, is explicitly delegated by the Board of Directors of the Baptist Memorial Health Care Corporation who acts solely as the contracting and internal management agent for all of its affiliated healthcare facilities.

The Baptist IRB is authorized to:

1. Review, approve, require modifications (to secure approval) or disapprove research activities involving human participants, human data or biospecimens, including exempt research activities under 45 CFR 46.104 of the revised Common Rule for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii) and (d)(3)(i)(C);
2. To require that informed consent is obtained and documented in accordance with regulatory and policy requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB.

   The IRB may require that information, in addition to that specifically mentioned in the regulations, 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;

3. For research subject to the revised Common Rule (2018 requirements): To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in Section 10;

   When research is subject to other regulations (e.g., pre-2018 Common Rule, FDA, DOJ) or requirements (e.g., grant or contract terms) that require continuing review, the IRB will conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year.

4. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
5. To observe, or have a third party observe, the consent process;
6. To observe, or have a third party observe, the conduct of the research
7. Where appropriate, determine that adequate additional protections are ensured for vulnerable populations such as fetuses, pregnant women, prisoners, and children, as required by Subparts B, C and D of 45 CFR § 46.

8. To determine whether data or specimens gathered without IRB approval or in association with serious or continuing noncompliance may be published or used for research purposes.

9. To oversee the conduct of human subject research that qualifies for exempt status and to take action as needed to ensure the protection of human subjects and the integrity of the research.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of Baptist. However, those officials may NOT approve research if it has not been approved or has been disapproved by the IRB. Reviewing officials may strengthen requirements and/or conditions, or add other modifications before approval, or may require approval by an additional committee, office, or person. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating any changes or modifications that result from such additional organizational reviews.

Additionally, the Baptist IRB is authorized to function as the Privacy Board for purposes of complying with the research provisions of regulations at 45 CFR §§ 160 and 164.

In its review of human participant research, the IRB has jurisdiction over all aspects of the research including, but not limited to:

1. Methods of identifying potential subjects;
2. Methods proposed for contacting potential subjects;
3. Materials to recruit subjects and proposed compensation;
4. Pilot studies;
5. Proposals to use or provide stored blood, tissues, or confidential data;
6. Surveys and questionnaires;
7. The informed consent process and forms;
8. The protocol and summary of the research;
9. Evaluation of risks and benefits to subjects;
10. Unanticipated problems involving risk to subjects;
11. Proposed changes to the research;
12. Continuing reviews;
13. Use of investigational drugs and devices in emergencies;
14. Humanitarian use of drugs and devices; and
15. Eligibility for exemption or expedited review.

9.2 Independence of the IRB

The IRB functions independently. The IRB must remain free from the influence of financial and other organizational interests. No individual with responsibility for the business and financial interests of the organization may serve on the IRB.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of Baptist. However, Baptist officials may not approve research that has not been approved by the Baptist IRB or by an approved external IRB. (45 CFR § 46.112; 21 CFR § 56.112)

9.3 Undue Influence

It is Baptist's policy that IRB review processes, and the implementation of its policies and procedures, are to be conducted objectively and without undue influence over deliberations or processes. Any effort by any party to influence the staff or members of the IRB is not allowed. Undue influence may take the form of threats about employment status, offers of money or other items of value or intimidating behavior. (45 CFR § 46.112)

9.3.1 Reporting Undue Influence

IRB staff and IRB members must report attempts to exert undue influence to the IRB Chair, the Executive Director, the Corporate Compliance Officer or the Baptist Helpline/Hotline (1-877-BMH-TIPS). Any individual may report such attempts.

9.3.2 Baptist Response to Attempts to Exert Undue Influence

Reports received via Section IV above will be reviewed. The outcome of the review will be documented, the complainant provided with a response, and a corrective action plan instituted if deemed necessary.

9.4 IRB Oversight

All research involving human subjects conducted at any facility affiliated with Baptist or by an employee or agent of Baptist is subject to review and oversight by the Baptist IRB.

A third-party IRB may be used in instances where there is a Reliance Agreement on file designating another IRB of record.
The Assistant Director or designee has the authority to determine which studies may use a third-party IRB and reserves the right to be able to require any study to be subject to the Baptist IRB review at any point of the study's lifecycle, even if a third-party IRB has previously reviewed and approved the study. (See Section 6)

9.5 Roles and Responsibilities

9.5.1 Chair of the IRB

- The Institutional Official appoints the Chair and Vice Chair in renewable five-year terms. Any change in appointment, including reappointment or removal, requires written notification.

- The IRB Chair should be a highly respected individual fully capable of managing the IRB, and the matters brought before it, with fairness and impartiality. The task of making the IRB a respected part of the research community falls primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial and immune to pressure by administration, the investigators whose research plans are brought before it, and other committees and professional and nonprofessional offices/sources.

- The IRB Chair or Vice Chair is responsible for conducting the meetings, conducting expedited reviews and may serve as signatory for correspondence generated by the IRB.
- The IRB Chair or Vice Chair is authorized to take immediate action to suspend a study or studies if information is presented regarding subject safety or for any other reason where such action would be deemed appropriate. Such action requires subsequent notice to and review by the convened IRB.

- The IRB Chair may designate other experienced IRB members to perform duties such as expedited reviews and other IRB functions.

- The IRB Chair advises the Institutional Official (IO) and the HRPP Assistant Director about IRB member performance and competence. The performance of IRB Chair will be reviewed on an annual basis by the IO in consultation with the Assistant Director. Feedback from this evaluation will be provided to the Chair. If the Chair is not acting in accordance with the IRB's mission, or following these policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Chair, he/she may be removed.

9.5.2 Vice Chair of the IRB

- The Vice Chair serves as the Chair of the IRB in the absence of the Chair and has the same duties as the Chair.

- The performance of IRB Vice Chair will be reviewed on an annual basis by the IO in consultation with the IRB Chair and Assistant Director. Feedback from this evaluation will be provided to the Vice Chair. If the Vice Chair is not acting in accordance with the IRB's mission, or following these policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the Vice Chair, he/she may be removed.

9.5.3 IRB Members

The role of an IRB member is to ensure that human research activities comply with federal regulations, state and local laws, and organizational policies and procedures, by:

- Completing member education and training, both initial and on-going;

- Maintaining the confidentiality of IRB deliberations and research review by the IRB;
- Conducting and documenting reviews of assigned research in a timely fashion;
- Attending IRB meetings as scheduled;

- Recusing self from final deliberations and vote when s/he has a conflict of interest;

- Participating in subcommittees of the IRB if requested and available; and
- Conducting themselves in a professional and collegial manner.

Members should attend all the meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the IRB Coordinator.

If an IRB member is to be absent for an extended period of time, he or she must notify the IRB Coordinator in advance so that an appropriate alternate/replacement can be obtained. If the member has a designated alternate, the alternate can serve during the primary member's absence.

The performance of IRB members will be reviewed on an annual basis by the IRB Chair and Vice Chair in consultation with the HRPP Assistant Director. IRB members will receive formal documented feedback on the results of this review. Members who are not acting in accordance with the IRB's mission or not following policies and procedures or who have an undue number of absences may be removed.

Alternate Members

The appointment and function of alternate members is the same as that for primary IRB members. An alternate's expertise and perspective should be comparable to those of the primary member. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member received or would have received.

The IRB roster identifies the primary member(s) or class of members (e.g., physician scientist) for whom each alternate member may substitute. The alternate member will not be counted toward meeting quorum as a voting member unless the primary member is absent. The IRB minutes will document when an alternate member replaces a primary member.

Experienced alternate members may be designated by the Chair or Vice Chair to conduct expedited reviews.

Subcommittees of the IRB

The IRB Chair, in consultation with the Assistant Director, may designate one or more other IRB members to a subcommittee of the IRB to perform duties, as appropriate, and undertake other IRB functions, and to make recommendations to the IRB (e.g., to supplement the IRB's initial review, continuing review, review of modifications, and/or review of reports of unanticipated problems or of serious or continuing non-compliance). The IRB Chair, in consultation with the Assistant Director, will appoint IRB members to serve on each IRB Subcommittee created under this Section.

The number and composition of the IRB Subcommittee members shall depend on the

scope of duties delegated by the IRB Chair to such IRB Subcommittee (e.g., making recommendations, conducting an inquiry, etc.). Any such Subcommittee cannot approve research that requires approval at a convened IRB meeting.

9.6 IRB Membership

The structure and composition of the Baptist IRB is appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most of the research performed at the Baptist.

The IRB will include members who are knowledgeable about and experienced working with vulnerable populations that typically participate in Baptist research.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. Baptist has procedures that specifically outline the requirements of research plan review by individuals with appropriate scientific or scholarly expertise. A member of the IRB may fill multiple membership position requirements for the IRB.

9.7 Composition of the IRB

The IRB will have at least five members, with at least one M.D., with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution.

The IRB shall be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

The IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas.

If the IRB regularly reviews research that involves subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration shall be given to the inclusion of one or more individuals on the IRB, who are knowledgeable about and experienced in working with these categories of subjects.

Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the organization's consideration of qualified persons of both sexes, so long as no selection is made to the IRB solely on the basis of gender. The IRB shall not consist entirely of members of one profession.

The IRB includes:

- At least one member whose primary concerns are in scientific areas;
- At least one member whose primary concerns are in nonscientific areas.
- At least one member who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization.
- At least one member who represents the general perspective of participants.

One member may satisfy more than one membership category.

The IRB Chair and Vice-Chair are voting members of the IRB and the staff of the Baptist IRB Office may be voting members of the IRB.

Individuals involved with business operations, grants management, the development office or technology transfer may not serve as members of the IRB or carry out day-to-day operations of the IRB. Individuals from these positions may provide information to the IRB and attend IRB meetings when invited as guests.

On an annual basis, the IRB Chair and the Assistant Director shall review the membership and composition of the IRB to determine if they continue to meet regulatory and organizational requirements. Members will receive documented feedback on their performance as reviewers following this annual review.

9.8 Appointment of IRB Members

When the IRB Chair and/or Assistant Director identifies a need for a new, replacement, or alternate member, the names of candidates will be sent to the Assistant Director. Chairs may forward nominations to the Institutional Official, or to the Assistant Director for consideration. The final decision in selecting a new member is made by the Institutional Official, in consultation with the IRB Chair and the Assistant Director.

Appointments are renewable terms. Any change in appointment, including reappointment or removal before the end of a member's term, requires written notification. Members may resign by written notification to the Chair or Assistant Director.

On an annual basis, the IRB Chair and the Assistant Director review the membership and composition of the IRB to determine if they continue to meet regulatory and institutional requirements.

9.9 Liability Coverage for IRB Members

The Baptist insurance coverage applies to employees and any other person authorized to act on behalf of Baptist for acts or omissions within the scope of their employment or authorized activity.

9.10 IRB Registration Updates

Changes in IRB membership will be reported to FDA and OHRP as follows:

- A Baptist decision to disband a registered IRB that it is operating will be reported in writing within 30 days after permanent cessation of the IRB's review of DHHS-conducted or supported research.
- If an FDA-regulated IRB decides to review additional types of FDA- regulated products (e.g., to review device studies if it only reviewed drug studies previously) or to discontinue reviewing clinical investigations regulated by FDA, it must report this within 30 days of the changes.
- Within 90 days after changes regarding the contact person who provided the IRB registration information or the IRB Chair.
- To register any additional IRB before it is designated under an FWA and reviews research conducted or supported by DHHS or regulated by the FDA.
- Within 90 days of a change in the membership roster if that IRB is designated under an FWA.

9.11 Use of Consultants

When necessary, the IRB Chair or the Assistant Director may solicit Individuals from the organization or the research community with competence in special areas to assist in the review of issues or research plans, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB. The IRB Office will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

Prospective consultants who are not employed by Baptist will be asked to agree in writing to:

- Keep confidential the subject matter and their involvement in the review process.
- Confirm that they have no personal or scientific conflict of interest that would prevent giving an unbiased opinion; and
- Confirm that neither they nor members of their immediate family have any financial interest in the study or sponsor.

Written statements from consultants will be kept in the IRB records. Key information provided by consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer will be filed with the study records.

The consultant's findings will be presented to the convened board for consideration either in person, via telephone, or in writing. If in attendance, these individuals will provide consultation and may assist in the deliberation but may not participate in the vote.

Ad hoc or informal consultations requested by individual members (rather than the convened board) will be processed by the IRB Office in a manner that protects the investigator's confidentiality and is in compliance with the IRB conflict of interest policy.

10 IRB Actions, Failure to Respond, Appeals

10.1 IRB Actions

In conducting its review of research, the IRB may take any of the following actions. With the exception of disapproval, the actions listed below may be used for either expedited or convened board review, including limited IRB review under the 2018 requirements. An action of disapproval can only be taken at a convened IRB meeting.

Approval

- The research, proposed modification to previously approved research, or another item is approved. The IRB has made all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). No further action is needed.

Conditions Required for Approval

- The research, proposed modification to the previously approved research, or other item is approved but conditions must be satisfied before the approval becomes effective. The date of IRB approval is the date that the Chair or designee confirms that the conditions are satisfied and becomes the start of the approval period.

- The IRB may approve research with conditions if, given scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.)). Any time the IRB cannot make one or more of the determinations required for approval, the IRB may not approve the study with conditions.

- The IRB may require the following as conditions of approval of research:

    1. Confirmation of specific assumptions or understanding on the part of the IRB regarding how the research is to be conducted (e.g., confirmation that research excludes children);

    2. Submission of additional documentation (e.g., certificate of training);

    3. Precise language changes to the study, consent, or other study documents; or

    4. Substantive changes to the study, consent, or other study documents along with clearly stated parameters that the changes must satisfy.

- When the IRB approves research with conditions, the conditions are documented in the IRB minutes for research reviewed at a convened meeting or in the Reviewer Checklist for research reviewed under an expedited review procedure.

- When the convened IRB approves research with conditions, the IRB may designate

the IRB Chair (and/or other qualified individual(s)) to review responsive materials from the investigator and determine that the conditions have been satisfied. If the conditions have not been satisfied, or are only partially satisfied, the responsive materials must be referred to the convened IRB for review. When an expedited reviewer approves research with conditions, the original expedited reviewer (and/or other qualified individual(s)) receives the response materials.

- After verification, the following is documented in IRB records and written communication to the investigator:

    1. The date when verification was made that all IRB conditions have been satisfied (i.e., the "effective date");

    2. For initial approval, the date when approval becomes effective (i.e., the date on which the investigator's response has been accepted as satisfactory), and;

    3. The date by which continuing review must occur (i.e., the expiration date).

    4. The IRB is informed of the outcome of the review of the investigator's response either at a convened meeting of the IRB or via IRB Information Items.

Partial Approval

- The IRB may stipulate that certain component of the research, which the IRB has determined to meet the criteria for approval, may commence or continue while other components of the research that require modification or clarification cannot begin or continue until the outstanding issues are resolved and approved by the convened IRB. For example, the IRB could determine that a study may begin but that children cannot be enrolled until the investigator submits, and the IRB approves, a plan for assent.

Deferral

- This action is taken by the IRB when modifications are required (of the nature or amount that the full IRB cannot make or specify exact changes or parameters), or additional information or clarification is needed in order to determine that one or more criteria for approval are satisfied (e.g., the risks and benefits cannot be assessed with the information provided).

- The deferral and the basis for the deferral is documented in the IRB minutes (for convened review) or Reviewer Checklist (for expedited review) and are communicated to the investigator in writing.

- When the convened IRB defers approval, the responsive materials from the investigator are provided to the convened IRB for review at a subsequent meeting. When an expedited reviewer defers approval, the original expedited reviewer reviews the response materials whenever possible. In the event that the original expedited reviewer is unavailable, the response is reviewed by the IRB Chair or other qualified IRB member who has been designated to conduct expedited review.

Disapproval of a Study

- The IRB may determine that the proposed research cannot be conducted at Baptist or by employees or agents of Baptist or otherwise under the auspices of Baptist. Disapproval can only be decided at the convened IRB meeting. An expedited reviewer cannot disapprove a study.

Approved in Principle

- As per federal regulations, [45CFR46.118], there are circumstances in which a sponsoring agency may require certification of IRB approval as a condition of submitting for or releasing funds but before definitive plans for the involvement of human subjects have been developed (e.g., certain training grants or grants in which the procedures involving human subjects are dependent on the completion of animal studies or instrument development). In these circumstances, the IRB may grant "approval in principle" without having reviewed the as yet undeveloped procedures or materials. The IRB Chair or designee reviews the available information (i.e., the grant or proposal and any supplemental information provided by the investigator) and, if appropriate, provides certification of IRB approval in principal. If the proposal is funded, the investigator must submit such materials for approval at least [60] days before recruiting human subjects into the study, or into any pilot studies or pre-tests.

- In addition to the above actions, the IRB may acknowledge reports and other items that don't involve prospective changes to already approved research. For example, the IRB may acknowledge the report of a protocol deviation but approve, require modifications in, or disapprove any associated corrective action plan. Further, the IRB may approve an item but include comments noting certain requirements, restrictions, or understandings. For example, with collaborative research, the IRB may note that approval must also be obtained from another IRB with jurisdiction and that the letter documenting that approval must submitted to the Baptist IRB before human research activities involving the collaborating organization or personnel may commence.

10.2 Failure to Respond

Upon review of a research study, the IRB may require changes or request certain information from an investigator. Failure to respond to IRB required changes or requests for information within 60 days (or fewer if the IRB determines that the information must be submitted earlier to ensure protection of the research subjects) may result in suspension or termination of IRB approval for the study. For studies that have not yet been approved, the study submission may be administratively withdrawn. At its discretion, the IRB may grant an extension beyond 60 days if the investigator contacts the IRB office prior to the deadline and presents sufficient cause for delay.

10.3 Reporting IRB Actions

All IRB actions are communicated to the investigator, and/or designated contact person for the

research study, via the publication of a notification in the IRB electronic system within ten (10) working days, whenever possible, of the review. When applicable, a stamped copy of the approved consent form, parental permission form, and/or assent form will also be published. For IRB actions of conditions required for approval or deferral, the notification will include a listing of the conditions or requirements that must be satisfied or responded to. For a disapproval, suspension, or termination, the notification will include the basis for the action and will offer the investigator an opportunity to respond in person or in writing.
The IRB reports its findings and actions to the organization in the form of its minutes, which are distributed by IRB staff to the Baptist IO.

10.4 Appeal of IRB Decisions

When the IRB suspends, terminates, or disapproves research, the IRB letter communicating the decision will include the basis for the action and will offer the investigator the opportunity to respond in person or in writing. Additionally, whenever an investigator disagrees with an IRB requirement or decision or believes that providing the IRB with additional information may result in a different outcome, they may request that the IRB reconsider its decision by submitting a memo and other supportive materials via the IRB electronic system. The investigator may be invited to attend the IRB meeting to discuss the request and provide information but will be asked to leave prior to the IRB's final deliberations and vote.

11 The IRB Review Process

11.1 Expedited Review

An IRB may use the expedited review process to review the following:

- For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations or other requirement that requires reviewer determination of minimal risk:
    - When the research activities involve only procedures appearing on the federal register list (or when applicable, the FDA list) of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk.
- For research subject to the 2018 Common Rule:
    - When the research activities involve only procedures appearing on the federal register list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk. If the reviewer determines that the research involves more than minimal risk, the reviewer must document the rationale for the more than minimal risk determination and the research must be reviewed by the convened IRB.
    - Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii) and (d)(3)(i)(C).
- Minor changes in previously approved research during the period (of one year or less) for which approval is authorized. Note: review of minor changes does not alter the end-date of study approval

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--used by the Baptist IRB.

11.1.1 Definitions:

Minimal Risk: 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 examinations or tests.

Minor Change: A minor change is one which, in the judgment of the Baptist IRB reviewer, makes no substantial alteration in:

- The acceptability of the risk-to-benefit analysis or increases the level of risks to subjects.
- The research design or methods (adding procedures that are not eligible for expedited review would be considered more than a minor change).
- The number of subjects enrolled in the research (usually not greater than 10% of the

total requested locally).

- The qualifications of the research team (i.e., the change does not negatively impact the expertise available to conduct the research).
- The facilities available to support safe conduct of the research.
- Any other factor which would warrant review of the proposed changes by the convened IRB.

Minor changes also include the addition of sites to a protocol approved by the convened IRB so long as the investigator(s)/site(s) do not have a conflict of interest, potential compliance concerns (e.g., a Form FDA 483 Inspectional Observations that has not been resolved adequately), or any other investigator or site-specific concerns (e.g., qualifications, facilities, or resources to safely conduct the research)

Quorum: A quorum of the Baptist IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non- scientific area. When research involving an investigational new drug or device is on the agenda for review, a physician should be included in the quorum.

Suspension of IRB approval: A suspension of Baptist IRB approval is a directive of the IRB to temporarily stop some or all previously approved research activities. Suspended research studies remain open and require continuing review.

Termination of IRB approval: A termination of Baptist IRB approval is a directive of the convened IRB to permanently stop all activities in a previously IRB approved research study. Terminated research studies are closed and no longer require continuing review.

11.1.2 Categories of Research Eligible for Expedited Review

The Baptist IRB applies the categories of research eligible for expedited review, which were published in the Federal Register on November 9, 1998 (Common Rule: notice 63 FR 60364-60367; FDA: notice 63 FR 60353).

The categories in this list apply regardless of the age of subjects, except as noted in category 2.

The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The expedited review procedure may not be used for government classified research involving human subjects.

Research Categories one (1) through seven (7) may be used for both initial and continuing IRB review:

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
    a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugsthat significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

    b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

    a. from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or

    b. from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it is collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week. (Note: Children are defined as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.)

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include:

    a. hair and nail clippings in a non-disfiguring manner;

    b. deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

    c. permanent teeth if routine patient care indicates a need for extraction;

    d. excreta and external secretions (including sweat);

    e. un-cannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue;

    f. placenta removed at delivery;

g. amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

h. supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

i. mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

j. sputum collected after saline mist nebulization;

k. vaginal swabs that do not go beyond the cervical os; and

l. rectal swabs that do not go beyond the rectum.

4. Collection of data through noninvasive procedures, not involving general anesthesia or sedation, routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. NOTE: Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications. Examples include:

   a. physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

   b. weighing or testing sensory acuity;

   c. magnetic resonance imaging;

   d. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography;

   e. moderate exercise, muscular strength testing, body composition assessment; and

   f. flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis). NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects.

See Exempt Categories and 45 CFR 46 101(b)(2) and b(3). This listing refers only to research that is not exempt.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior); or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.

Categories 8 and 9 apply only to continuing review:

8. Continuing review of research previously approved by the convened IRB as follows:

    a. Where (i) the research at Baptist is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects NOTE: "Long-term follow-up" includes research interactions that involve no more than minimal risk to subjects (e.g., quality of life surveys), and collection of follow-up data from procedures or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research study, but not interventions that would not have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.; or

    b. Where no subjects have ever been enrolled at Baptist and no additional risks have been identified NOTE: "no additional risks have been identified" means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB's most recent prior review; or

    c. Where the remaining research activities at Baptist are limited to data analysis. NOTE: Simply maintaining individually identifiable private information without using, studying, or analyzing such information is not human subject research and thus does not require continuing review.

9. Continuing review of research previously approved by the Baptist IRB at a convened meeting that meets the following conditions:

    a. The research is not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE);

    b. Expedited review categories (2) through (8) do not apply to the research;

    c. The IRB has determined and documented at a convened meeting that the research, or the remaining research activity involving human subjects, involves no greater than minimal risk to the subjects; and

    d. No additional risks of the research have been identified. NOTE: "no additional risks have been identified" means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB's most recent prior review.

11.1.3 Expedited Review Procedures

IRB members are not selected, and/or do not participate in the expedited review of research in which they have a conflict of interest but may answer questions about the research if requested.

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the Chair from among members of the Baptist IRB. IRB members who serve as designees to the IRB Chair for expedited review are matched as closely as possible with their field of expertise to the study.

On an annual basis, the Chair or Vice Chair designates a list of Baptist IRB members eligible to conduct expedited review. The designees must be experienced (having served on the IRB for at least one year) voting members or alternate members of the IRB. The IRB Staff selects expedited reviewers from that list. Selected reviewers should have the qualifications, experience and knowledge in types of research to be reviewed, as well as be knowledgeable of the requirements to approve research under expedited review. IRB members with a conflict of interest in the research are not selected.

When reviewing research under an expedited review procedure, the IRB staff provides to the IRB Chair or designee(s) all documentation that would normally be submitted for a full-board review. This requirement applies to all categories of submissions including initial reviews, continuing reviews, and modifications.

If the research meets the criteria allowing review using the expedited procedure, the reviewer(s) conducting initial or continuing review completes the appropriate review form checklist (Initial Review Checklist, Continuing Review Checklist, Modifications Review Checklist) to confirm that the activity can be reviewed by the

expedited process, and to determine whether the research meets the regulatory criteria for approval. The same criteria of approval apply to reviews conducted via expedited review as to those conducted by the convened board. If the research does not meet the criteria for expedited review, then the reviewer indicates that the research requires full review by the Baptist IRB and the research study is placed on the next available agenda for an IRB meeting.

In reviewing the research, the reviewers follow the review procedures and may exercise all of the authorities of the Baptist IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure by the convened IRB.

Reviewers indicate approval, required modifications or requirement for convened board review on the appropriate checklist (initial, continuing, modification) and return it to the IRB Office where it is kept with the study file. If modifications are required, the IRB Office staff informs the investigator in writing.

In the event that expedited review is carried out by more than one IRB member and the expedited reviewers disagree, the IRB Chair may make a final determination or the study is referred to the convened IRB for review.

Informing the Baptist IRB: All members of the IRB will be apprised of all expedited review approvals, including limited IRB reviews conducted using expedited review procedures, by means of a list in the agenda for the next scheduled meeting. Any IRB member can request to review any study by contacting the IRB Office.

11.2 Convened IRB Meetings

Except when an expedited review procedure is used, the Baptist IRB conducts initial and continuing reviews of all non-exempt research (and exempt research subject to limited IRB review if not otherwise expected) at convened meetings at which a quorum (see below) of the members is present.

11.2.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year (usually twice per month). The schedule for the IRB may vary due to holidays or lack of quorum. The schedule for IRB meetings is posted on the Baptist IRB website. Special meetings may be called at any time by the Chair or designee or the Assistant Director of the Baptist HRPP.

11.2.2 Preliminary Review

The Baptist IRB Coordinator performs a preliminary review of all submissions for determination of completeness and accuracy. Only complete submissions are placed on the IRB agenda for review. The investigator is informed either by e-mail, phone or in person of missing materials and the necessary date of receipt for inclusion on the agenda. If an investigator is submitting for the first time or is not well-versed in the submission procedures, consultations can be arranged with IRB staff.

11.2.3 Primary and Secondary Reviewers

After it has been determined that the submission is complete, the IRB Coordinator, with the assistance of the IRB Chair or designee(s) as needed, assigns submissions for review paying close attention to the subject matter of the research, the potential reviewer's area/s of expertise and representation for any vulnerable populations involved in the research. One "primary reviewer" is assigned to each submission and receives and reviews the full submission materials. A reviewer may be assigned several submissions or other items for review. When the IRB is presented with a research study which may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant is sought. Research studies for which appropriate expertise cannot be obtained for a given meeting are deferred to another meeting when appropriate expertise is available.

Primary reviewers are responsible for:

1. Having a thorough knowledge of all of the details of the proposed research.
2. Performing an in-depth review of the proposed research.
3. Beginning the discussion of the proposed research at the convened meeting, by summarizing the proposed research, and leading the IRB through the regulatory criteria for approval.
4. Making suggestions for changes to the proposed research, where applicable.
5. Completing all applicable IRB reviewer forms.

One or more "secondary" reviewers may be assigned in addition to the primary reviewer. A secondary reviewer may be assigned to review the full submission materials or may be asked to review specified sections of the submission (e.g., the consent/assent/permission forms). All assigned reviewers are required to complete the Reviewer Checklist in advance of the IRB meeting.

All IRB members receive and are expected to review all studies, not just those assigned as primary [or secondary] reviewers.
When it can be anticipated that the primary reviewer may be absent from the meeting, a new primary reviewer may be assigned, providing that they have sufficient time to review the materials in advance of the meeting. Additionally, an absent reviewer can submit their written comments for presentation at the convened meeting. If an absent reviewer submits comments, those can indicate a recommendation regarding approval, but such recommendation is not counted as a vote.

11.2.4 Materials Received by the Baptist IRB

All required materials need to be submitted to the IRB office 14 days prior to the convened meeting for inclusion on the IRB agenda. The meeting agenda is prepared by the IRB coordinator in consultation as needed with the IRB Chair or Vice-Chair. All IRB members receive the IRB agenda, prior meeting minutes, applicable business items, continuing education materials and research submission materials no later than 5 business days before the

scheduled meeting to allow sufficient time for the review process. On occasion, a time-sensitive item may be added to the agenda if circumstances warrant and the IRB staff have contacted the IRB members and verified that they will have sufficient time for review.

Each IRB member receives and reviews the following documentation, as applicable, for all studies on the agenda:

- A Protocol/Research Plan Summary or the complete Protocol (Detailed description of the research proposed; background, description of the research, methods, etc.)
- The Study Application (Applicable IRB Manager X-Form)
- Proposed Consent/Parental Permission/Assent Form(s)
- Recruitment materials including advertisements intended to be seen or heard by potential subjects
- Any other subject materials, such as questionnaires or diaries

In addition to the above, the primary reviewers receive and review

- the full protocol/research plan,
- any relevant grant applications; and,
- the investigator's brochure (when one exists) and/or other risk information.

Additionally, for HHS-supported multicenter clinical trials, the primary reviewer should receive and review a copy of the HHS- approved sample informed consent document(s) (when one exists) and the complete HHS-approved protocol/research plan (when one exists).

The materials provided to the primary reviewer are available to all members. Any IRB member may request any of the materials provided to the reviewers by contacting the IRB Office.

If an IRB member requires additional information to complete the review, they may contact the investigator directly or may contact the IRB Office to make the request of the investigator.

11.2.5 Quorum

A quorum of the Baptist IRB consists of a majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. When research involving an investigational new drug or device is on the agenda for review, a physician should be included in the quorum. At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote.

The IRB Chair, with the assistance of the IRB staff, confirms that a quorum is present before calling the meeting to order. The IRB Chair, with the assistance of the IRB staff, ensures that the IRB meeting remains appropriately convened. If a quorum is not maintained, either by losing a majority of the members, losing all non-scientific members or another required member, the IRB cannot take further actions or vote on regulatory determinations until

quorum is restored.

It is generally expected that at least one unaffiliated member and at least one member who represents the general perspective of participants (one individual can serve in both capacities) is present at all IRB meetings. The IRB may, on occasion, meet without this representation; however, this should be the exception.

If the IRB regularly reviews research with subjects vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, or individuals with impaired decision-making capacity or economically or educationally disadvantaged persons, one or more individuals (e.g., IRB members, alternate members, or consultants) who are knowledgeable about and experienced with those subjects should be present during the review of the research.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting. Whether or not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent members that are transmitted by mail, telephone, facsimile or e-mail may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

11.2.6 Meeting Procedures

The Baptist IRB Chair calls the meeting to order once it has been determined that a quorum is in place. The Chair reminds IRB members to recuse themselves from the discussion and votes by leaving the room when they have a conflict. The IRB reviews and discusses the minutes from the prior meeting and determines if there are any revisions/corrections to be made. If there are no changes to be made, the minutes are accepted as presented and considered final. If major revisions/corrections are necessary, the minutes are amended and presented at the following IRB meeting. Minor revisions/corrections may be verified by the IRB Chair or Vice-Chair outside of the convened meeting.

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The Reviewer presents an overview of the research and can assist the Chair in leading the IRB through the completion of the regulatory criteria for approval in the Institutional Review Board Study Review checklist. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

When the IRB is presented with a research study which may be outside of the knowledge base or representative capacity of the IRB members, an outside consultant is sought. Research studies for which appropriate expertise cannot be obtained for a given meeting is deferred to another meeting when appropriate expertise is available.

It is the responsibility of the IRB coordinator to record the proceedings of the session. In addition, the IRB coordinator is responsible for taking Minutes at each IRB meeting.

11.2.7 Guests

Investigators and research staff may be invited to the Baptist IRB meeting, at the discretion of the IRB, to make a brief presentation or to answer questions about proposed or ongoing research. The investigator/research staff may not be present for the deliberations or vote on the research.

The ED and staff regularly attend IRB meetings and may participate in the IRB discussion and deliberations but may not vote.
Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair, Vice Chair and the Assistant Director. Such guests may be asked to sign a confidentiality agreement and do not participate in discussion unless requested by the IRB, under no circumstances may they vote.

11.3 Criteria for Baptist IRB Approval of Research

In order for the IRB to approve human subjects research, either through expedited review or by the convened IRB, it must be determined that the following requirements are satisfied. These criteria apply to all categories of IRB reviews including initial reviews, continuing reviews, and modifications of previously approved research.

1. Risks to subjects are minimized:

    a. by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and

    b. whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research is conducted. The IRB should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

4. Informed consent is sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations [45 CFR 46.116/21 CFR 50].

5. Informed consent will be appropriately documented, or appropriately waived, in accordance with, the Federal Regulations [45 CFR 46.117/21 CFR 50].

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

For purposes of conducting the limited IRB review required by 45 CFR46.104 (d) (7), shall make the following determinations: (i) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of 45 CFR 46.116 (a)(1)-(4), (a)(6), and (d); (ii) Broad consent is appropriately documented or waiver of documentation is appropriate in accordance with 45 CFR 46.117; and (iii) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

11.3.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health or other direct benefit for the research subjects, justifies asking any person to undertake the risks; and
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

- **Identify the risks** associated with the research, as distinguished from the risks of activities, diagnostic tests, treatments, or therapies the subjects would receive even if not participating in research;

- **Determine whether the risks are minimized** to the extent possible by evaluating the necessity of procedures that impart risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impart less risk;

- **Identify the anticipated benefits** to be derived from the research, both direct benefits

to subjects and possible benefits to society, science and others;

- **Determine whether the risks are reasonable in relation to the benefits**, if any, and assess the importance of the knowledge to be gained;

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research - as distinguished from risks and benefits subjects would receive even if not participating in the research.
The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks and benefits that fall within the purview of its responsibility.

11.3.1.1 Scientific or Scholarly Review

In order to assess the risks and benefits of the proposed research, the IRB must determine that:

1. The research uses procedures consistent with sound research design; and
2. The research design is sound enough to reasonably expect the research to answer its proposed question.

In making this determination, the IRB may draw on its own knowledge and expertise, or the IRB may draw on the knowledge and expertise of others, such as reviews by a funding agency, or departmental review. When scientific or scholarly review is conducted by an individual or entity external to the IRB, documentation that the above questions were considered must be provided to the IRB for review and consideration.
Scientific or scholarly review can be delegated to a departmental or other appropriate review committee.

11.3.2 Equitable Selection of Subjects

The Baptist IRB determines by reviewing the application, protocol/research plan and other materials that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB does not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- The purposes of the research;
- The setting in which the research occurs;
- Scientific and ethical justification for including subjects who are vulnerable to coercion or undue influence such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons;
- The scientific and ethical justification for excluding classes of persons who might benefit from the research; and

- The inclusion/exclusion criteria and the procedures/materials intended for use for the identification and recruitment of potential subjects.

At the time of the continuing review the IRB determines that the investigator has followed the subject selection criteria that were originally set forth at the time of the initial IRB review and approval.

11.3.2.1 Recruitment of Subjects

The investigator provides the Baptist IRB with a plan for recruitment of all potential subjects. All recruiting materials are submitted to the IRB, including advertisements, flyers, scripts, information sheets and brochures. The IRB should ensure that the recruitment plan and materials appropriately protect the rights and welfare of the prospective subjects (e.g., do not present undue influence).

See Section 11.4 for a discussion of IRB review of advertisements and payments to subjects.

11.3.3 Informed Consent

The Baptist IRB ensures that informed consent is sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB ensures that informed consent is appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27.

The IRB ensures, as part of its review, that the information in the consent document and process is consistent with the research plan, and, when applicable, the HIPAA authorization.

11.3.4 Data and Safety Monitoring

For all research that is more than minimal risk, the investigator should submit a data and safety monitoring plan. The initial plan submitted to the Baptist IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the monitoring results to the IRB. Data safety monitoring may be performed by a researcher, medical monitor, safety monitoring committee, or other means. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB reviews the safety monitoring plan and determines if it makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects and address problems that may arise over the course of the study. If a plan was not submitted, the IRB determines whether or not a plan is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study.

The factors the IRB considers in determining whether the safety monitoring plan is adequate for the research are as follows:

- Monitoring is commensurate with the nature, complexity, size and risk involved.
- Monitoring is timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB.
- For low risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.
- For greater-than-minimal-risk studies that do not include a plan for monitoring by a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), and that are blinded, multi-site, involve vulnerable populations, or involve high-risk interventions or procedures, the IRB will carefully evaluate the proposed Data Safety Monitoring Plan and may require establishment of a DSMB, DMC, or other methods to enhance the monitoring and management of participant safety.

Data and Safety Monitoring plans should specify:

- The entity or person(s) who perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator
- The safety information that is collected and monitored, including serious adverse events and unanticipated problems
- The frequency or periodicity of review of safety data
- The procedures for analysis and interpretation of the data
- The procedures for review of scientific literature and data from other sources that may inform the safety or conduct of the study
- The conditions that trigger a suspension or termination of the research (i.e., stopping rules), if applicable
- The procedures for reporting to the IRB, including a summary description of what information, or the types of information, that is provided

For a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), the plan should describe:

- The composition of the board or committee. Generally, a DSMB should be composed of experts in all scientific disciplines needed to interpret the data and ensure subject safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease/condition and treatment under study should be part of the monitoring group or be available if warranted.

- Frequency and content of meeting reports
- The frequency and character of monitoring meetings (e.g., open or closed, public or private)
- The Charter should be provided, when one exists

In general, it is desirable for a DSMB or DMC to be established by the Study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions.

For some studies (e.g., multi-site clinical trials involving interventions that entail potential risk to the participants) the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB or DMC as a condition for approval of research where it determines that such monitoring is needed.

When DSMBs or DMCs are used, IRBs conducting continuing review of research may rely on a current statement, or the most recent report, from the DSMB or DMC which indicates that it has and continues to review study-wide adverse events, study wide interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

11.3.5 Privacy and Confidentiality

The Baptist IRB will determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

11.3.5.1 Definitions

- Confidentiality: Methods used to ensure that information obtained by investigators about subjects is not improperly divulged.
- Privacy: Having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. It is the state or condition of being free from unauthorized intrusion, being observed or disturbed by other people.
- Identifiable private information: Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- Identifiable Biospecimen: A biospecimen for which the identity of the subject is or may be readily ascertained by the investigator or associated with the biospecimens.
- Private information: Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).

- Sensitive Information: data or information, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, unauthorized access, misuse, alteration, or loss or destruction of the information (e.g., could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation).

11.3.5.2 Privacy

The IRB must determine whether the activities in the research appropriately protect the privacy of potential and actual subjects. In order to make that determination, the IRB must obtain information regarding how the investigators plan to access subjects or subjects' private, identifiable information and the subjects' expectations of privacy in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration is given to:

- Methods used to identify and contact potential participants
- Settings in which an individual may be interacting with an investigator
- Appropriateness of all personnel present for research activities
- Methods used to obtain information about participants, and the nature of the requested information including minimizing the information obtained to achieve the aims of the research
- Information that is obtained about individuals other than the "target subjects," (e.g., a subject provides information about a family member for a survey) and whether such individuals meet the regulatory definition of "human subject"

11.3.5.3 Confidentiality

The IRB must determine if appropriate protections are in place to minimize the likelihood that information about subjects may be inappropriately divulged. Safeguards designed to protect confidentiality should be commensurate with the potential of harm from unauthorized, inappropriate or unintentional disclosure.

At the time of initial review, continuing review and with any requests for modification, the IRB assesses whether there are adequate provisions to protect data confidentiality. The IRB does this through the evaluation of the methods used to obtain, record, share, and store information about individuals who may be recruited to participate in studies and about subjects. The investigator provides the IRB with a plan regarding the procedures to be taken to protect the confidentiality of research data and sensitive information. Additionally, the investigator provides information regarding information

security procedures and plans to address the protection of paper documents, other physical media (e.g., audio or videotapes), and electronic data and information including the use, maintenance, storage, and transmission of information. The IRB reviews all information received from the investigator and determine whether or not the confidentiality of research data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data.

In reviewing confidentiality protections, the IRB considers whether or not the data or other information accessed or gathered for research purposes is sensitive and the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. It evaluates the effectiveness of proposed de-identification techniques, coding systems, encryption methods, methods of transmission, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections. In reviewing confidentiality protections, the IRB also considers regulations and organizational requirements and policies regarding the use of information and information security.

Research regulated by the FDA that involves the use of electronic data collection/storage systems must comply with the requirements of 21 CFR Part 11.

11.3.6 Vulnerable Populations

Certain individuals, by nature of their age or mental, physical, economic, educational, or other situation, may be more vulnerable to coercion or undue influence than others. At the time of initial review, the Baptist IRB considers the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Section 15.

11.4 Additional IRB Considerations

11.4.1 Determination of Risk

At the time of initial and continuing review, the Baptist IRB will make a determination regarding the risks associated with the research plan. Risk determinations may vary over the life of a research plan depending on the procedures and risks that subjects will be exposed to as the research progresses. The level of risk associated with the research influences eligibility for expedited review. The meeting minutes will reflect the convened IRB's determination regarding risk levels; expedited reviewers will document the determination of risk level on the reviewer checklist.

11.4.2 Period of Approval

At the time of initial review and at continuing review, the IRB will make a determination

regarding the frequency of review of the study.

For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations: The IRB will conduct continuing review of research at intervals appropriate to the degree of risk but not less than once per year.

For research subject to the revised Common Rule (2018 requirements): The IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described in 45 CFR §46.109(f)(1)

All FDA-regulated studies will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. In some circumstances, a shorter review interval (e.g., semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below). The meeting minutes will reflect the convened IRB's determination regarding review frequency; expedited reviewers will document the determination of risk level on the reviewer checklist.

IRB approval is considered to have lapsed at midnight on the expiration date of the approval (i.e., the expiration date is the last day research can be conducted). For a new study reviewed by the IRB, the approval commences on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB or expedited reviewer approves the research **or** the date ("effective date") that it is verified that the requirements of the IRB have been satisfied following an action of Approval with Conditions. When continuing review is required, the expiration date of the initial approval period, which is the date by which the first continuing review must occur, may be as late as one year after the effective date of initial IRB approval.

The use of the effective date of IRB approval to determine the latest permissible date for continuing review *only applies to the first continuing review*. For all subsequent continuing reviews of a research study subject to convened board review, the date the convened IRB or the date that the expedited reviewer conducts continuing review and approves the study (with or without conditions) determines the latest permissible date of the next continuing review (when continuing review is required).

The approval date and approval expiration date, when applicable, are clearly noted on IRB determination letters and must be strictly adhered to. Investigators should allow sufficient time for development and review of continuing review submissions. As a courtesy, the HRPP Office will send reminders to the investigator prior to the study's expiration date, notifying him or her that the study is due for a continuing review or when approval has expired.

IRB review of a proposed modification to research ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full research project, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires. If the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain

the anniversary date as the date by which the continuing review must occur.

The IRB may determine continuing review is not required in the following circumstances:

- Research eligible for expedited review in accordance with 45 CFR 46.110
- Research reviewed by the IRB in accordance with the limited IRB review described in 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8);
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
- Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

11.4.3 Review More Often Than Annually

The following factors will be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical/psychological/social/legal/educational condition of the proposed subjects.
3. The overall qualifications of the investigator and other members of the research team.
4. The specific experience of the investigator and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events observed in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events/unanticipated problems more likely.
7. The involvement of especially vulnerable populations likely to be subject to undue influence or coercion (e.g., terminally ill)
8. A history of serious or continuing non-compliance on the part of the investigator.
9. Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of subjects studied or enrolled determines the approval period only when that

number of subjects is studied or enrolled in less than one year (unless the study does not require continuing review). If an approval period of less than one year is specified by the IRB, for research that is subject to continuing review, the reason for more frequent review must be documented in the minutes or the expedited reviewer's checklist.

11.4.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB use sources other than the investigator to independently verify that no material changes occurred during the IRB- designated approval period.

The IRB determines the need for verification from outside sources on a case-by-case basis. The following factors are considered when determining which studies require independent verification:

- The nature, probability and magnitude of anticipated risks to subjects;
- The degree of uncertainty regarding the risks involved;
- Whether the research involves novel therapies or procedures;
- The vulnerability(ies) of the subject population;
- The projected rate of enrollment;
- The experience and expertise of the investigators;
- The IRB's previous experience with the investigators or the sponsor (e.g., compliance history, complaints from subjects, etc.);
- The probable nature and frequency of changes that may ordinarily be expected in the type of research;
- Whether the research undergoes routine independent monitoring;
- Whether concerns about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources; and
- Any other factors that suggest independent verification is warranted.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period or may require such verification at the time of any other review (e.g., continuation, modification, interim reports) or when a complaint, concern, or allegation is received.

If any material changes have occurred without IRB review and approval, the IRB reviews for non-compliance and takes appropriate action.

11.4.5 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (e.g., consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

- High risk studies;
- Studies that involve particularly complicated procedures or interventions;
- Studies involving highly vulnerable populations (e.g., ICU patients, children who are wards);
- Studies involving study staff with minimal experience in administering consent to potential study participants; or
- Other situations when the IRB has concerns that consent process may not be/is not being conducted appropriately (e.g., prior investigator non-compliance, etc.).

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB Chair, Vice Chair, or designee develops a monitoring plan and submits it to the IRB for approval. The consent monitoring may be conducted by HRPP staff, IRB members, or a research participant advocate, either affiliated or not with Baptist. The investigator is notified of the IRB's determination and the reasons for the determination. Arrangements are made with the investigator for the monitoring of the consent process, typically for a specified number of subjects. When observing the consent process, the monitor determines:

- Whether the informed consent process was appropriately conducted and documented;
- Whether the participant had sufficient time to consider study participation;
- Whether the consent process involved coercion or undue influence;
- Whether the information was accurate and conveyed in understandable language; and
- Whether the subject appeared to understand the information and gave their voluntary consent.
- Helping legally authorized representatives (LAR) obtain information from investigators and others and to assist LAR in making decisions on behalf of the subject;
- Reporting to the IRB concerns regarding the consenting process or subject safety and the views of the subjects when appropriate.

11.4.6 Investigator Qualifications

The IRB may review credentials, curriculum vitae, resumes, or other relevant materials to determine whether investigators and members of the research team are appropriately qualified to conduct the research. The IRB relies upon other Baptist credentialing processes to inform this determination.

11.4.6.1 Individuals External to Baptist Who Request to Conduct Research at Baptist

On occasion, individuals who are not affiliated with BCHCC, including but not limited to private practice physicians, nursing students and researchers at other institutions, request Baptist IRB approval for their research. Additionally, individuals may request access to patient data for research purposes. The following is BMHCC policy for these requests.

a. Requests for de-identified data.
   Typically, the desired data is stored in medical records and, as such, is restricted by HIPAA and internal BMHCC policy. Many times, the researcher requests data that can be released as part of de-identified data set under a data use agreement (DUA) negotiated with the BMHCC Privacy Office/Privacy Officer. Since the research does not use identifiable data, it can be classified as Non-Human Subject Research (NHSR) and does not require IRB approval.

b. Requests for identifiable data.
   There may also be requests for patient data that include one or more of the 18 HIPAA identifiers. Requests for identified data must be approved by the Privacy Office/Privacy Officer as a Limited Data Set with a DUA.

c. Requests for IRB review and approval of research.
   IRB review and approval of research from individuals not affiliated with BMHCC places the institution at increased liability. Since the individual is not an employee of Baptist, neither the institution nor the IRB has authority over that individual, nor can the Baptist IRB provide necessary regulatory oversight of the research and the researcher. Individuals not affiliated with BMHCC who wish to have the Baptist IRB be the IRB of Record must:

   1. Identify a BMHCC/BHSU faculty member to be a co-principal investigator or co-investigator on the research protocol.
   2. The IRB application must be submitted by the BMHCC/BHSU faculty member using the IRB Manager platform.
   3. The BMHCC/BHSU faculty member will be responsible for assuring regulatory compliance while the research is conducted, regardless of where the research is conducted.
   4. The non-affiliated individual must agree to periodic quality assurance audits, regardless of where the research is conducted, if requested by the IRB.

11.4.7 Significant New Findings

During the course of research, significant new knowledge or findings about the research, the test article, and/or the condition under study may develop. The investigator must report any significant new findings to the IRB and the IRB will review them and evaluate the impact on the subjects' rights and welfare. When the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require that the investigator contact subjects to inform them of the new information. The IRB will communicate this requirement to the investigator. If the study is still enrolling subjects, the consent document should be updated. The IRB may require that the currently enrolled subjects be re-consented or otherwise provided with the new information. When appropriate, the IRB may also require that former subjects be provided with the new information (e.g., late emerging safety information).

If potential subjects are scheduled for the consenting process while consent document(s) are under review by the IRB, the Investigator may continue to use the previously approved consent document(s) provided that IRB approval of the study has not lapsed and any proposed changes to the consent document are administrative in nature and do not change the risk profile of the study. Previously approved and non-expired consent document(s) may be used for the consent process until a newly approved and stamped consent document is made available to the Investigator. Any subjects who complete the consent process while proposed changes to study consent documents are under review by the IRB must complete the consent process again when/if the proposed changes are approved. The 're- consenting' process should occur within a period determined by the Board, but not to exceed thirty (30) days from the date the Investigator receives the Board's determination and stamped documents.

11.4.8 Conflicts of Interest (COI)

<u>Investigator Conflicts of Interest</u>

The IRB research application asks specific questions regarding the investigator and research team compliance with disclosure requirements and whether or not any COI management plans are in place. As part of its review process, the IRB will make a final determination as to whether any conflict of interest is adequately addressed and protects the human subjects in the research. For further information, see S.AD. 1006.

<u>Institutional Conflicts of Interest</u>

As with individual conflict of interest, the IRB has final authority to determine whether the Institutional Conflict, the Financial Interest, and the management plan, if any, allow the study to be approved.

11.4.9 Advertisements and Recruitment Materials

The Baptist IRB must review and approve any and all advertisements prior to posting and/or distribution for studies that are conducted under the purview of Baptist. The IRB reviews:

- The information contained in the advertisement.

- The mode/method of its communication.
- The final copy of printed advertisements.
- The proposed script and final audio/video taped advertisements.

This information should be submitted to the IRB with the initial application or, if recruitment is proposed after study approval, as a modification request.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate. This includes but is not limited to:

- Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the research plan.
- Claims, either explicitly or implicitly, that the test article (drug, biologic or device) is safe or effective for the purposes under investigation.
- Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device.
- Using terms like "new treatment," "new medication," or "new drug" without explaining that the test article was investigational.
- Promising "free medical treatment" when the intent was only to say participants are not to be charged for taking part in the investigation.
- Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media.
- Offers for a coupon good for a discount on the purchase price of an investigational product once it has been approved for marketing.
- The inclusion of exculpatory language.

Recruitment materials should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

- The name and address of the investigator and/or research facility.
- The condition being studied and/or the purpose of the research.
- In summary form, the criteria used to determine eligibility for the study.
- The time or other commitment required of the subjects.
- The location of the research and the person or office to contact for further information.

- A clear statement that this is research and not treatment.
- A brief list of potential benefits (e.g., a no-cost health exam).

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

Directory listings of research such as ClinicalTrials.gov are not considered advertisements and therefore do not require IRB review and approval if the listing is limited to the following basic trial information: title, purpose of the study, research plan summary, basic eligibility criteria, study site location(s), and how to contact the study site for further information.

The first contact prospective study subjects make is often with a person who follows a script to determine basic eligibility for the specific study. The IRB should ensure the procedures followed adequately protect the rights and welfare of the prospective subjects.

11.4.10 Payments to Research Subjects

Payment to research subjects may be an incentive for participation or a way to reimburse a subject for travel and other experiences incurred due to participation. However, payment for participation is not considered a research benefit. Regardless of the form of remuneration, investigators must take care to avoid unduly influencing subjects. The amount of compensation must be proportional to the time and inconveniences posed by participation in the study.

Investigators who wish to pay research subjects must submit to the IRB the amount and schedule of all payments. Investigators should indicate in their research project application the justification for such payment. Such justification should substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject and do not constitute (or appear to constitute) undue pressure on the potential subject to volunteer for the research study.

The IRB must review both the amount of payment and the proposed method and timing of disbursement to ensure that neither entails problems of coercion or undue influence.

Credit for payment should be prorated and not be contingent upon the participant completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it could unduly induce subjects to remain in the study when they otherwise would have withdrawn.

The consent form must describe the terms of payment, including the amount, method and schedule of payments and any conditions under which subjects would receive partial payment (e.g., if they withdraw from the study before their participation is completed) or no payment.

Unless the study is confidential, the Baptist Finance Department requires identifying information to issue checks, cash, or gift certificates to subjects. The consent form must inform subjects that they are asked to provide their Social Security Number and verification of U.S Citizenship or Permanent Resident Status to receive payment. For

confidential studies, only name and address are required by the Finance Department, but the investigator MUST keep an identity key in a secure place.

11.4.11 Non-Monetary Gifts and Incentives

Similar to financial incentives, non-monetary gifts or incentives can also present problems of undue influence or coercion that impact a potential subject's ability to fully and freely consider participation in research.

If subjects are provided with non-monetary gifts or tokens of appreciation, such as totes, books, toys, or other such materials, the approximate retail value must be described to the IRB and the IRB is provided with a description, photo, or sample product to review.

The IRB reviews all gifts and incentives being particularly sensitive to the influence of power or authority, whether perceived or actual, over free decision-making. Overt coercion (e.g., threatening loss of credit, or access to services or programs, to which the potential subjects are otherwise entitled) is never appropriate. Moreover, it must be clear that choosing to not participate will not adversely affect an individual's relationship with the organization or its staff or the provision of services in any way (e.g., loss of credits or access to programs).

Investigators should carefully structure incentives and methods of disbursement so that while the incentives may serve as a factor in a subject's decision to participate, that they have not served to unduly influence or coerce participation.

11.4.12 State and Local Laws (See Section 1.11.13)

The Baptist IRB considers and adheres to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and IRB rely on the Baptist Counsel for the interpretation and application of the laws of any other jurisdiction where research is conducted as they apply to human subject research. The IRB ensures that consent forms are consistent with applicable state and local laws.

11.5 Continuing Review

For research subject to the pre-2018 Common Rule, FDA or DOJ regulations, and any research where continuing review is required by applicable regulations, policy, or other requirements:

The IRB will conduct continuing review of research at intervals appropriate to the degree of risk but not less than once per year. The date by which continuing review must occur will be recorded in the IRB record and on initial and continuing review approval letters. There are no exceptions to the requirement for continuing review in the pre-2018 Common Rule, or in FDA or DOJ regulations.

The IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described below. When applicable, the date by which the continuing review must occur will be recorded in the IRB record and on initial and continuing review approval letters.

Unless an IRB determines otherwise, continuing review of research subject to the 2018 Common Rule (the revised Common Rule) is not required in the following circumstances:

- Research eligible for expedited review in accordance with 45 CFR 46.110;
- Research reviewed by the IRB in accordance with the limited IRB review;
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
    a. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
    b. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Baptist IRB may determine that continuing review is required for any research protocol that falls within the above criteria. For example, the IRB may determine that continuing review is required when:

- Required by other applicable regulations (e.g., FDA);
- Required by the terms of a grant, contract, or other agreement;
- Recommended by Federal guidance (e.g., OHRP recommends that IRB's require continuing review of research that falls within expedited categories 8(b) and 9);
- The research involves topics, procedures, or data that may be considered sensitive or controversial;
- The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;
- An investigator has minimal experience in research or the research type, topic, or procedures; and/or
- An investigator has a history of noncompliance.

When the Baptist IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

Studies that are determined to not require continuing review are still subject to prompt reporting requirements (e.g., proposed amendments, unanticipated problems involving risk to subjects or others, protocol deviation, violations, non-compliance). They will also require submission of an annual progress report that will collect information regarding status of the research activity. Investigators will receive courtesy reminder e-mail notices for completion of the progress report. Research Compliance staff will review the report for compliance with institutional policies (verification of human subjects training, COI review, etc). Failure to submit an annual progress

report as required will constitute non-compliance with Baptist's HRPP policy and may result in suspension of the study until compliance with this policy is confirmed.

11.5.1 Continuing Review Process

As a courtesy to investigators, the IRB Office staff sends out renewal notices to investigators at 60 days in advance of the expiration date; however, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Investigators must submit the following for continuing review:

- The initial study application form updated with any changes (this serves as the protocol/research plan summary);
- The current protocol/research plan;
- The current Investigator's Brochure or other updated risk information (if applicable);
- The most recent report from the DSMB or DMC (if applicable);
- The most recent multi-center progress report (if applicable);
- Any proposed modifications to the protocol/research plan, consent, or study; and
- The continuing review application form (progress report)
- Reports of any internal audits by Corporate Compliance (if not already reviewed by the IRB)

Baptist IRB Office staff attends the convened meetings and bring the complete study files for each study on the agenda. IRB members can request the study file or any additional materials from the IRB staff prior to the meeting.

In the case of expedited review, the reviewer may request that the IRB office staff provide them with any additional materials required for their review.

11.5.2 IRB Considerations for Continuing Review

In order to re-approve research at the time of continuing review, the IRB determines that the regulatory criteria for approval continue to be satisfied. Because the research was previously found to satisfy the criteria for approval, the IRB focuses its considerations at the time of continuing review on whether any new information is available that would affect the IRB's prior determination that the criteria for approval are satisfied. The IRB pays particular attention to four aspects of the research:

- Risk assessment and monitoring;
- Adequacy of the informed consent process; including that the current consent document is still accurate and complete and any significant new findings that arise

from the review process and that might relate to participants' willingness to continue participation is provided to participants;

- Local investigator and organizational issues; and
- Research progress.

11.5.3 Convened Board Review

In conducting continuing review of research not eligible for expedited review, all Baptist IRB members are provided with access to all of the materials listed in Section 11.5.1 and are responsible for reviewing the project summary, the current consent document, the progress report, and, if applicable, the data and safety monitoring report, multi-center study progress reports, and any proposed modifications to the protocol/research plan, or consent. The Primary Reviewer is responsible for reviewing the complete materials submitted for continuing review including the complete research plan and is given access to the complete IRB file and relevant IRB meeting minutes. All assigned reviewers are responsible for completing a reviewer checklist in advance of the convened meeting. At the meeting, the Primary Reviewer (and secondary when assigned) assists the Chair by providing a summary of the research, their evaluation of the research and continuing review materials, and recommendations.

11.5.4 Expedited Review

In conducting continuing review under expedited procedures, the reviewers receive all of the previously noted materials. The reviewer(s) complete the Reviewer Checklist for Continuing Review of Research to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

For research subject to the pre-2018 Common Rule, or FDA or DOJ regulations: Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) (see Expedited Review Categories). It is also possible that research activities that previously qualified for expedited review have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

For research subject to the revised Common Rule (2018 requirements): Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, unless it has progressed to the point that it involves only one or both of the following:

- Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care; and
- in limited circumstances described by expedited review categories (8) and (9).

When continuing review is not required for research subject to the 2018 Common Rule and the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale in the checklist.

11.5.5 Possible IRB Actions after Continuing Review

As with Initial Review, at the time of Continuing Review, the Convened Baptist IRB or IRB Member(s) conducting expedited review may take any of the following actions:

- Approval
- Conditions Required for Approval
- Deferral

Additionally, the convened IRB may vote to disapprove the study. If an IRB member conducting expedited review believes that the study should be disapproved, it is referred to the convened board for review. If the IRB has significant concerns, the IRB may vote to suspend approval or terminate the research (See Section 12).

If a research study receives Approval with Conditions at the time of the Continuing Review, the IRB specifies whether any conditions need to be satisfied before an investigator can continue particular research activities related to those conditions or requirements that must be adhered to until the conditions of approval have been satisfied. For example, if at the time of continuing review, the IRB requires the investigator to change the research protocol to include a specific new procedure for screening prospective subjects, the IRB could approve the research with the following condition: "*Research activities involving currently enrolled subjects may continue, but no new subjects may be enrolled until a designated IRB member reviews a revised protocol and verifies that the protocol includes the new screening procedure*."
Additionally, the IRB may specify a time period, such as 1, 2, or 3 months, for the conditions to be satisfied as long as the activity with conditions is not begun/restarted until approval is granted.

11.5.5 Lapses in Approval

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired is research conducted without Baptist IRB approval. If re-approval does not occur within the time set by the IRB, all research activities must stop, including recruitment (media advertisements must be withdrawn), enrollment, consent, interventions, interactions, and data collection. This occurs even if the investigator has provided the continuing information before the expiration date. **Therefore, investigators must submit their continuing review materials enough in advance of expiration to allow sufficient time for IRB review before the expiration date.**

The lapse of IRB approval due to a failure to complete continuing review and obtain re-

approval prior to expiration of the prior approval does not ordinarily constitute a suspension or termination of IRB approval, for federal reporting purposes; however, the failure to meet continuing review obligations may be grounds for suspension or termination of the research. If the IRB notes a pattern of non-compliance with the requirements for continuing review (e.g., an investigator repeatedly or deliberately neglects to submit materials for continuing review in a timely fashion or the IRB itself is not meeting the continuing review dates), the IRB should determine the reasons for the non-compliance and take appropriate corrective actions. The IRB must report to FDA/OHRP any instance of serious or continuing non-compliance with FDA regulations or IRB requirements or determinations. When the IRB approves research with conditions at the time of continuing review before the expiration date of the preceding IRB approval period, IRB approval does not lapse if the investigator needs additional time – beyond the date on which the preceding IRB approval would have expired – to satisfy some or all of the IRB's conditions. However, the investigator and the IRB should make every effort to resolve any conditions and finalize approval in as timely a manner as possible.

11.5.6.1 Management of Enrolled Subjects During the Lapse of Approval

The IRB Office is responsible for notifying the investigator of the expiration of approval and that all research activities must stop. However, the IRB recognizes that, while enrollment of new subjects cannot occur after the expiration of IRB approval, temporarily continuing participation of already enrolled subjects may be necessary or appropriate, for example, when the research interventions hold out the prospect of direct benefit to the subjects, or when withholding those interventions or safety monitoring procedures, would place subjects at increased risk. In these instances, the investigator should, at the earliest opportunity, contact the IRB office and submit a request to continue those research activities that are in the best interests of subjects. Such a request should specifically list the research activities that should continue, and provide justification, and indicate whether the request applies to all or only certain subjects. The IRB Chair or designee will review the request and provide a determination regarding what activities, if any, may continue during the lapse. Such a determination may include a time limit or other conditions or restrictions. If the IRB decides that already enrolled subjects should continue to receive the interventions that were being administered to subjects under the research project, data collection (especially safety information) should also continue for such subjects.

When there is insufficient time to obtain an IRB determination (e.g., the study regimen includes daily administration of an investigational agent), the investigator may make an initial determination, in consultation with the subjects' treating physician, if appropriate. In such cases, the investigator must, as soon as possible, contact the IRB office and submit a request for confirmation that the IRB agrees with the determination. The IRB Chair or designee reviews the request and provides a determination. In the event that the IRB does not agree with the investigator's determination, or only agrees in part (e.g., agrees that some but not all of the activities are in the best interests of subjects), the IRB notifies the investigator who must then comply with the IRB's requirements or request a re-review of the determination by providing additional justification or information that the IRB may not have considered.

A study may be closed administratively after 60 days if the IRB has not received information from the investigator. If the investigator wishes to re-open the study, full board review may be required or as consistent with the initial review process.

11.6 Modification of an Approved Protocol

Investigators may wish to modify or amend their approved applications. Investigators must seek Baptist IRB approval before making any changes, no matter how minor, in approved research - even though the changes are planned for the period for which IRB approval has already been given – unless the change is necessary to eliminate apparent immediate hazards to the subject (in which case the IRB must then be notified at once).

Modifications may be permanent (Protocol Modification) which make changes to the protocol for all remaining subjects or temporary (Protocol Exceptions – See Section 11.6.5) circumstances in which the specific procedures called for in a protocol are not in the best interests of a specific patient(s)/subject(s) (examples: patient/subject is allergic to one of the medications provided as supportive are; patient/subject is not eligible in a direct benefit study). Usually, a Protocol Exception is a change that is planned and has prior agreement from the sponsor.

Investigators should consider whether the proposed changes to the research alter the original scope, purpose, or intent of the research. When the research itself is fundamentally changed, the IRB will typically require a new study application rather than allow such changes to be made through a modification to the existing research plan.

11.6.1 Procedures

Before implementing any changes, investigators must first request and obtain IRB approval by submitting to the IRB:

- For Protocol Modifications, log in the IRB Manager a, select the study to be revised, select the protocol form and select “Copy to Amend”. The original protocol wil be archived by the system and the amended protocol will show tracked changes when submitted and until the modifications are approved by the IRB;
- Revised consent/parental permission/assent documents (if applicable) or other documentation proposed to be provided to subjects; and
- Any other relevant documentation, including documents provided by the sponsor or coordinating center.

IRB Office staff reviews the submission and make an initial determination whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants convened board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the research study for convened board review.

11.6.2 Convened Board Review of Modifications

When a proposed change in a research study is not minor, or when a proposed change to an expedited study renders it no longer eligible for expedited review, the Baptist IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

All IRB members are provided and review all documents provided by the investigator. The primary reviewer will complete the modification review checklist.

At the meeting, the Primary Reviewer presents an overview of the proposed modifications and assists the IRB Chair in leading the IRB through the completion of the regulatory criteria for approval. The IRB determines whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB considers whether information about those modifications might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to future/current/past participants.

11.6.3 Expedited Review of Modifications

The Baptist IRB may use expedited review procedures to review minor changes in ongoing previously approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or experienced designee(s) among the IRB members.

Expedited reviewers complete the modifications review checklist to determine whether the modifications meet the criteria allowing review using the expedited procedure, and, if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval. The reviewer(s) will also evaluate whether the modification alters any previous determinations (e.g., a Subpart determination), or necessitates any additional determinations (e.g., for vulnerable populations).

The reviewer also considers whether information about those modifications might relate to future/current/past participants' willingness to continue to take part in the research and if so, whether to provide that information to participants.

11.6.4 Possible IRB Actions after Modification Review

As with Initial Review, at the time of Continuing Review, the Convened Baptist IRB or IRB Member(s) conducting expedited review may take any of the following actions:

- Approval
- Conditions Required for Approval
- Deferral

Additionally, the convened IRB may vote to disapprove the proposed changes. If an IRB member conducting an expedited review believes that the proposed modifications should be disapproved, they refer the proposed modification to the convened board for review. If the proposed changes raise significant concerns on the part of the IRB, the IRB may vote to suspend or terminate the research.

11.6.5 Protocol/Research Plan Exceptions

> Protocol/Research Plan exceptions are circumstances in which the investigator wishes to deviate from eligibility criteria or one or more of the specific procedures called for in a research plan. Unlike modifications that apply to all subsequent subjects in the research, a protocol/research plan exception only applies to a specific subject or group of subjects.

Exceptions are planned, and the investigator gets approval from the sponsor and the Baptist IRB ahead of time. For sponsored research, prior approval from the sponsor is generally required. Depending on the nature of the exception, an expedited review is possible. In order to be approved under expedited review exceptions must not increase risk or decrease benefit, change the risk/benefit analysis, negatively affect the participant's rights, safety, welfare, or negatively affect the integrity of the resultant data. Review of exceptions that represent more than minor changes or risks levels greater than minimal must be done at a convened meeting of the IRB.

Procedures for exceptions are the same as for a Protocol Modification. The investigator must submit a "Modification Request Form" along with any revised documentation to be presented to the subject(s) and documentation of sponsor approval, if applicable.
The only time a protocol/Research Plan exception would not require prior sponsor or IRB approval is when the exception is necessary to avoid an immediate hazard to the participant. In such cases, the exception must be submitted to the IRB as soon as possible.

11.7 Closure of Research Studies

The completion or early termination of the study, is a change in activity and must be reported to the Baptist IRB. Although subjects may no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Studies may be closed when the involvement of human subjects ceases (interventions, interactions, observations, and the gathering, use, study, and analysis of identifiable private information, including specimens, are all complete). Studies may be closed when the only remaining research activity involves the analysis of unidentifiable individual level data, or aggregate data sets.

For multi-center research, the study may be closed once all research activities (as above) are complete at Baptist and any sites for which the IRB is the "IRB of record". If the investigator is serving as the lead investigator or Baptist is the coordinating center, please note that the study must remain open as long as the coordinating center is still receiving, studying, using,

or analyzing identifiable private information from other sites (even if local interventions, interactions, observations, and data gathering is complete).

Investigators must submit study closures to the IRB. With closure submissions, the investigator must provide a summary of the research activity and any findings available at that time.

Investigators may maintain the data that they collected, including identifiable private data, if this is consistent with the IRB-approved research plan. However, investigators may not conduct any additional analysis of identified data without re-applying for IRB approval. Investigators must continue to protect the confidentiality of the data as described to the IRB and honor any other commitments that were agreed to as part of the approved research including, for example, future use of data or specimens, provision of research results to subjects, and provision of any outstanding payments or compensation.
The IRB will review study closure reports, typically by expedited review, and either approve the closure of the study or request additional information or confirmation of facts from the investigator.

11.8 Reporting IRB Actions

All Baptist IRB actions are communicated to the investigator, and/or designated contact person for the research study, in writing within ten (10) working days via a template letter prepared by the IRB staff. For an approval, along with written notification of approval, a copy of the approved consent, assent, permission forms (if applicable) containing the IRB stamp with the dates of the approval and expiration are sent to the investigator. For approval with conditions, the notification includes a listing of the conditions that must be satisfied. For a deferral, the notification includes the modifications and/or clarifications required along with the basis for requiring those modifications. For a disapproval, termination or suspension, the notification includes the basis for making that decision and give the investigator an opportunity to respond in person or in writing.

The IRB reports its findings and actions to the organization in the form of its minutes, which are distributed by IRB staff to the Baptist Institutional Official.

12 Suspensions, Terminations and Investigator Holds

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects. (See Section 17 for a discussion of unanticipated problems and Section 18 for a discussion of noncompliance.) The IRB's authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

12.1 Suspension

Suspension of IRB approval is a directive of the convened IRB or IRB Chair or Vice Chair to temporarily stop some or all previously approved research activities. Suspensions made by the IRB Chair or Vice Chair must be reported to IRB members at a convened IRB meeting. Suspended research studies remain open and require continuing review. Investigators must continue to provide reports on adverse events and unanticipated problems to both the IRB and sponsors, just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period).

When approval of some or all research activities is suspended by the IRB, the IRB will consider notification of subjects and any actions necessary to ensure that the rights, safety, and welfare of subjects are appropriately protected.

The IRB will notify the investigator in writing of suspensions and will include a statement of the reasons for the IRB's actions and any requirements or conditions associated with the suspension (e.g., notification of subjects). The investigator of a suspended study will be provided with an opportunity to respond in person or in writing.
Suspensions of IRB approval must be reported promptly to the Assistant Director and Institutional Official (IO), sponsors including federal department or agency heads, and federal oversight agencies according to applicable federal and organizational requirements. Institutional suspension or termination of research studies approved by the IRB can also be issued by Organization officials acting outside of and/or unrelated to the interests of the IRB. Such Organization actions can be made by, for example, the IO, Chief Compliance Officer and Chief Executive Officer. The investigator must report any suspension or termination of the conduct of research by organization officials to the IRB. The IRB will then determine if suspension or termination of IRB approval is warranted

12.2 Termination of IRB Approval

Termination of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research study. Terminated research studies are closed and no longer require continuing review. Terminations of IRB approval of research studies must be made by the convened IRB. When study approval is terminated by the IRB, in addition to stopping all research activities, the IRB will consider notification of subjects and any actions necessary to ensure that the rights, safety, and welfare of subjects are appropriately protected.

The IRB will notify the investigator in writing of a study termination and will include a statement

of the reasons for the IRB's actions and any requirements associated with the termination (e.g., notification of subjects). The investigator of a terminated study will be provided with an opportunity to respond in person or in writing.
Terminations of IRB approval must be reported promptly to the Executive Director and the IO, sponsors including federal department or agency heads, and federal oversight agencies according to applicable federal and organizational requirements. Note: Suspension or termination of research studies approved by the IRB can also be issued by Organization officials acting outside of and unrelated to the interests of the IRB. Such Organization actions can be made by, for example, the IO, Chief Compliance Officer and Chief Executive Officer. The investigator must report any suspension or termination of the conduct of research by organization officials to the IRB. The IRB will then determine if suspension or termination of IRB approval is warranted.

12.3 Investigator Hold

An investigator may request an "investigator hold" when the investigator wishes to temporarily or permanently stop some or all approved research activities. Such a hold is initiated by an investigator but must be immediately reported to the IRB so that the IRB can consider whether any additional actions are necessary to protect subjects. Investigator holds are not equivalent to IRB suspensions or terminations.

12.3.1 Procedures

Investigators must submit a memo and any supporting materials via the IRB electronic system to inform the IRB of the hold. The memo and materials should include:

1. A statement that the investigator is voluntarily placing a study on hold;
    a. The reason(s) for the hold;
    b. A description of the research activities that will be stopped;
    c. Proposed actions to be taken to protect current participants; and
    d. Any actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate risk of harm.

Upon receipt, IRB staff notify the IRB Chair or designee and place the research on the next available agenda for review;
The IRB Chair or designee, in consultation with the investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current participants;
The IRB Chair or designee, in consultation with the investigator, determines whether and how currently enrolled subjects will be notified of the hold;
Prior to lifting the hold, the investigator must seek approval from the IRB so that the IRB may consider whether subjects are appropriately protected and if the research remains approvable.

12.4 Protection of Currently Enrolled Participants

Before a study hold, termination, or suspension, is put into effect the Chair, Vice- Chair, or convened IRB considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring participants to another investigator/site.
- Making arrangements for clinical care outside the research.
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

13 Documentation and Records

Baptist IRB prepares and maintains adequate documentation of the IRB's activities. All records are accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

13.1 IRB Records

The IRB records are maintained in a manner that contains a complete history of all IRB actions related to review and approval of a protocol, including continuing reviews, amendments and unanticipated problems. IRB Records include, but are not limited to:

1. Written operating procedures
2. IRB membership rosters.
3. IRB member files, including documentation of appointments, experience, education/training, and expertise
4. Training records documenting that investigators, IRB members, and IRB staff have fulfilled Baptist's human subject protections training requirements
5. IRB correspondence including reports to regulatory agencies
6. IRB Study Records (Study Files) including correspondence with investigator and research team
7. Documentation of exemptions including exemptions related to emergency uses and when limited IRB review is a condition of exemption.
8. Minutes of convened IRB meetings, which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.
9. Records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in 45 CFR 46.109(f)(1).
10. Documentation of review by another institution's IRB when appropriate.
11. Documentation of IRB reliance and cooperative review agreements, e.g., Memoranda of Understanding (MOUs)
    a. For nonexempt research involving human subjects covered by the 2018 revised Common Rule (or exempt research for which limited IRB review takes place) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure

compliance with the requirements of this policy [the Common Rule] (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol);

12. Documentation of independent or external investigator agreements
13. Federal Wide Assurances
14. IRB Registrations
15. Documentation of complaints and any related findings and/or resolution.

13.2 IRB Study Files

The IRB maintains a separate IRB study file for each research application (including expanded access), Humanitarian Use Device (HUD), emergency use, or report it receives for review. Research studies are assigned a unique identification number. The study number is assigned by the electronic system. Accurate records are maintained of all communications to and from the IRB. Copies are kept electronically in the IRB electronic system. Baptist's IRB maintains a separate electronic file for each research study that includes, but is not limited to:

1. Research plan and all other documents submitted as part of a new study application including:
    i. Complete Initial Protocol Application form and all associated documents and materials;
    ii. Proposed and IRB-approved Consent / Parental Permission / Assent Form(s) (when applicable);
    iii. Recruitment materials / subject information (when applicable);
    iv. Data collection instruments (including all surveys and questionnaires);
    v. Investigator Brochure (when one exists) or Instructions for Use;
    vi. The complete protocol (when one exists);
    vii. HHS-approved sample consent form document and research plan (when they exist);
    viii. Documentation of scientific or scholarly review (if available).
2. Modification requests and all associated documents and materials;
3. Continuing Review/progress reports and all associated documents and materials, including the rationale for conducting continuing review of research that otherwise would not require continuing review under the revised Common Rule;
4. Closure reports and all associated documents and materials;

5. Documents submitted and reviewed after the study has been approved, including modification requests, protocol/research plan exception requests, proposed advertisements, data and safety monitoring reports, and reports of protocol/research plan violations, complaints, non-compliance, unanticipated adverse device events and unanticipated problems involving risks to subjects or others;
6. Documentation of types of IRB review. For exempt determinations and expedited review, this will include the category or basis under which the review is allowed;
7. For expedited review, documentation of any findings and determinations required by the regulations and study-specific findings supporting those determinations, including, but not limited to, waiver or alteration of consent, waiver of documentation of consent, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children. For research reviewed by the convened board these findings and determinations are recorded in the minutes;

8. For expedited review, documentation of the risk determination and period of approval. For research reviewed by the convened board these determinations are recorded in the minutes and, if applicable, the rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than minimal risk. For research reviewed by the convened board, the risk determination and period of approval, when applicable, are recorded in the minutes. Note: For FDA and DOJ-regulated research, the reviewer must still determine that the research is minimal risk;

9. Documentation of all IRB review actions;
10. Notification of expiration of IRB approval to the investigator and requirements related to the expiration;
11. Notification of suspension or termination of research;
12. Copies of approval letters and forms that describe any requirements that the investigator must satisfy before beginning the study;
13. IRB correspondence to and from research investigators;
14. All other IRB correspondence related to the research;
15. For studies evaluating the safety or effectiveness of medical devices, documentation of the determination by IRB of exempt, significant risk, or non-significant risk;
16. Reports of unanticipated problems involving risk to subjects or others;
17. Copies of reports of injuries to participants;
18. Data and safety monitoring reports, if any;
19. Significant new findings;
20. The justification for using the expedited procedure for continuing review of research, if

appropriate;
21. Documentation of audits, investigations, reports of external site visits.

13.3 IRB Meeting Minutes

A record of the proceedings of IRB meetings are written and available for review by the next regularly scheduled IRB meeting. Once accepted by the members, the minutes must not be altered by anyone including a higher organizational authority. A copy of IRB-approved minutes for each IRB meeting will be distributed to the IO.

Minutes of IRB meetings must contain sufficient detail to show:

1. Attendance
    a. Each member's (or alternate's) full name;
    b. Each member's (or alternate's) representative capacity (e.g., scientist, non-scientist, unaffiliated, member who represents the general perspective of research subjects);
    c. The names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending remotely received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;
    d. Names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for specific absent members or categories of members only as designated on the official IRB membership roster);
    e. Names of any consultants present, a brief explanation of their expertise, and documentation to support that the consultant(s) did not vote;
    f. The names of non-members and guests in attendance, such as IRB staff, investigators, and study coordinators;

    Note: The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect the numbers of members present for the vote on that item.
2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area;
3. When both a member and an alternate are present, the minutes will reflect if and when the alternate substituted for the member. Generally, the member votes, but an alternate may substitute when appropriate (e.g., the member has a conflict of interest, the alternate has needed expertise, etc.);
4. Business Items discussed, and any education provided;
5. Actions taken, including separate deliberations, actions, and votes for each submission undergoing review by the convened IRB;

6. Vote counts on these actions (Total Number Voting; Number voting for; Number voting against; Number abstaining; Number of those recused). When a member is recused due to conflict of interest, the name of the member and reason for the recusal will be noted;
7. Basis or justification for actions disapproving or requiring changes in research;
8. Summary of controverted issues and their resolution;
9. Approval period for initial and continuing reviews, when applicable, including identification of research that warrants review more often than annually and the basis for that determination;
10. For research subject to the revised Common Rule (2018 requirements): The rationale for requiring continuing review of research that otherwise would not require continuing review;
11. Risk determination for initial and continuing reviews, and modifications when the modification alters the prior risk determination;
12. Justification for deletion or substantive modification of information concerning risks or alternative procedures contained in the HHS- approved sample consent document;
13. Study-specific findings supporting that the research meets each of the required criteria when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent altogether;
14. Study-specific findings supporting that that the research meets each of the required criteria when the requirements for documentation of consent are waived;
15. Study-specific findings supporting that the research meets each of the criteria for approval for vulnerable populations under any applicable Subparts;
16. Exempt/significant risk/non-significant risk device determinations and the basis for those determinations;
17. Determinations related to conflicts of interest and acceptance or modification of conflict management plans;
18. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research;
19. Review and determinations related to interim reports (e.g., unanticipated problems or safety reports, serious or continuing noncompliance, suspensions or terminations, etc.);
20. A list of research approved under expedited review procedures, including limited IRB reviews conducted using expedited procedures, since the time of the last such report;
21. An indication that, when an IRB member or alternate has a conflicting interest with the research under review, the IRB member or alternate was not present during the final deliberations or voting; and
22. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant

13.4 IRB Membership Roster

A membership list of IRB members will be maintained; it will identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list will contain the following information about members:

1. Name;
2. Earned degrees;
3. Employment or other relationship between each member and the organization (i.e., affiliated or non-affiliated). To be categorized as non- affiliated, neither the member nor an immediate family member of the member may be affiliated with Baptist;
4. Status as scientist or non-scientist. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are considered a scientist for the purposes of the roster, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline are considered a nonscientist. Physicians, nurses, and pharmacists are considered scientists;
5. Indications of experience, such as board certifications, licenses, and areas of practice sufficient to describe each member's chief anticipated contributions to IRB deliberations;
6. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, adults with impaired decision making capacity, and other vulnerable populations or other subjects vulnerable to coercion or undue influence commonly involved in Baptist research;
7. Role on the IRB (Chair, Vice-Chair, etc.;
8. Voting status;
9. For alternate members, the primary member or class of members for whom the member could substitute.

The IRB office must keep the IRB membership list current. The Assistant Director or designee will report changes in the IRB Chair or contact person to OHRP/FDA within 90 days of the change.

13.5 Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer’s citation of a specific exemption category and written concurrence that the activity described in the investigator’s request for satisfies the conditions of the cited exemption category as detailed in Section 5. When an exemption includes limited IRB review under the revised Common Rule (2018 requirements), the documentation will include this fact and the IRB action taken on those aspects of the research subject to limited IRB review in accordance with the procedures described for the review

procedures used (expedited or convened board) elsewhere in these policies.

13.6 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category(ies) or status as exempt but requiring limited IRB review, documentation that the activity described by the investigator satisfies all of the criteria for approval; the approval period (when applicable) and any determinations required by the regulations including study- specific findings justifying the following determinations:

1. Approving a procedure which waives or alters the informed consent process;
2. Approving a procedure which waives the requirement for documentation of consent;
3. Approving research involving pregnant women, human fetuses, or neonates;
4. Approving research involving prisoners;
5. Approving research involving children.

13.7 Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

All IRB records are kept secure in locked filing cabinets, locked storage rooms, or on password protected computers. Doors to the IRB Offices are closed and locked when the rooms are unattended.

Ordinarily, access to all IRB records is limited to the Assistant Director, IRB Chair, IRB members, IRB staff, authorized organizational officials, and officials of federal and state regulatory agencies (e.g., OHRP and FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access. All other access to IRB records, including IRB member rosters, is limited to those who have legitimate need for them, as determined by the IO and the Assistant Director (and legal counsel as required).

Records may not be removed from the IRB Office; however, the IRB staff will provide copies of records for authorized personnel if requested.

IRB must make all records accessible for inspection and copying at reasonable times and in a reasonable manner.

Access to Baptist's electronic database, the Human Protocol System (HPS), is limited to appropriate Office of Research and BCRI staff. Electronic systems are frequently backed up and have a data recovery and disaster management plan.

For Department of Defense sponsored research there may be a requirement to submit records to the Department of Defense for archiving.

All other access to IRB study files is prohibited.

13.7.1 Requests for Copies of the IRB Roster

Occasionally, industry sponsors and others may request a copy of the IRB member roster. Access to IRB member rosters is limited to those who have legitimate need for them, as determined by the IO and the Assistant Director (and legal counsel as required).

Rather than provide a copy of the roster, a "Statement of Compliance" is provided to the requestor. The Statement affirms that the Baptist IRB is are organized and operates in compliance with U.S. federal regulations governing human subjects research including, when applicable, 45 CFR 46, 21 CFR Parts 50, 56, 312, and 812, and 45 CFR 164.512(i) and the reviews conducted by the Baptist IRB are guided by the ethical principles outlined in The Belmont Report. Also, when applicable, the Baptist IRB complies with the guidelines outlined in ICH GCP E6, to the extent that the guidelines are compatible with governing regulations.

In addition, the Statement refers to the Baptist Federalwide Assurance (FWA) and IRB registrations with OHRP and FWA.

The currency of Baptist's FWA and IRB registrations may be validated using the OHRP database at http://ohrp.cit.nih.gov/search.

13.8 Record Retention

In order to comply with the requirements of OHRP, FDA, and HIPAA, IRB records are maintained at the facility for at least six (6) years after completion of the research and are stored for ten (10) years total beyond the end of the calendar year in which the study is closed. Records may be stored electronically or on paper.

IRB records for research cancelled without participant enrollment will be retained at the facility for at least three (3) years after closure and are stored for ten (10) years total beyond the end of the calendar year in which the study is closed. Records may be stored electronically or on paper.

Administrative records (e.g., minutes, member lists, and budgets) are retained pursuant to federal regulations.

14 Obtaining Informed Consent

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the federal regulations and Baptist HRPP. Investigators are required to obtain legally effective informed consent from a subject or the subject's LAR unless the requirement has been waived by the IRB of record. When informed consent is required, it must be sought prospectively and properly documented. Except as provided in Sections 14.10, 14.11, and 14.12 of these procedures, informed consent must be documented using a written consent form approved by the IRB.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants. The informed consent process involves three key features: (1) disclosing to the prospective human subject information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the research. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach by an investigator and continuing through the completion of the research study. The process of obtaining informed consent must allow for a dialogue so that the potential subject has the opportunity to ask questions and receive responses. Investigators must obtain consent prior to entering a subject into a study, gathering data about a subject, and/or conducting any procedures required by the research plan, unless consent is waived by the IRB.

If someone other than the principal investigator obtains consent, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. Consent delegates must be knowledgeable about the research to be conducted and the consent process and must have the expertise be able to answer questions about the study including those regarding risks, procedures, and alternatives. The Baptist IRB application solicits information regarding who will obtain consent; proposed changes to the personnel authorized to obtain consent must be submitted to the Baptist IRB for approval. All Baptist studies must use the Baptist IRB consent template.

Sample or draft consent documents may be developed by a sponsor or network. However, the IRB of record is the final authority on the content of the consent documents that are presented to prospective subjects.
The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of Baptist.

14.1General Requirements

<u>For research subject to FDA or DOJ regulations.</u>

No investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. 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. The information that

is given to the subject or the representative shall be in language understandable to the subject or the representative. 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.

For research subject to the 2018 Common Rule

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR;
2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and 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 LAR shall be in language understandable to the subject or the LAR
4. The prospective subject or the LAR 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;
5. No informed consent may include any exculpatory language through which the subject or the LAR 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

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that have additional requirements for informed consent to be legally effective.
Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

14.2 Additional Requirements:

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, permission must be obtained from a legal guardian with appropriate authority to make decisions regarding the activities called for in the research or a legally authorized representative (LAR);

2. The informed consent process provides the prospective subject (or legally authorized representative) with sufficient opportunity to read the consent document, when applicable;

3. The informed consent process shall be sought under circumstances that provide the subject (or LAR) with sufficient opportunity to read, discuss, receive answers, and

consider whether or not to participate;

4. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence;

5. The informed consent information must be presented in language that is understandable to the subject (or LAR). To the extent possible, the language should be understandable by a person who is educated to the 8th grade level and layman's terms shall be used in the description of the research;
6. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or the subject's LAR). In accordance with this policy, the IRB requires that informed consent discussions include a reliable interpreter when the prospective subject does not understand the language of the person who is obtaining consent;

7. 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 participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

8. Informed consent as a whole must present information in sufficient detail relating to 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.

14.3 Legally Authorized Representative

A Legally Authorized Representative (LAR) is defined by 45 CFR 46.102(c) and 21 CFR 50.3 as *"an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research."* If there is no applicable law addressing this issue, LAR means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. Whoever may serve as LAR is determined by state law.
Tennessee law does not address who can be an LAR for research activities. Thus, the applicable guidelines for determining the most appropriate LAR for research are based upon the guidelines that apply in the clinical setting. The order of preference for who can serve as an LAR are as follows:

1. Court-appointed Conservator or Guardian of the individual with authority to make health care decisions for the patient

2. Person named in the patient's Durable Power of Attorney for Health Care (DPAHC)

3. If the subject does not have a court-appointed guardian or conservator and does not have a person authorized to act under a DPAHC, then both of the following must be true for an alternative adult to

serve as the LAR for this subject:

a. The LAR must be an individual who:

• Has exhibited special care and concern for the patient,

• Is familiar with the patient's personal values, and

• Is reasonably available to serve as a LAR.

When the Baptist IRB serves as the IRB of record for external sites and the use of LARs is proposed, information regarding relevant state law and local policy will be sought (local context information) and applied.
LARs should be well informed regarding their roles and responsibilities when asked to provide surrogate consent. In addition to the consent information, LARs should be informed that their obligation is to try to determine what the potential subject would do if able to provide consent, or if the potential subject's wishes cannot be determined, what they think is in the person's best interest.

Investigators must describe the intended use of LARs in their submission to the IRB. The IRB determines whether the use of LARs is appropriate for a given research study.

Further discussion and procedures for assessment of capacity and inclusion of adults with impaired decision-making capacity in research are described in Section 15.7.

14.4 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential subjects (or the subject's LAR):

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 that are experimental;

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

3. A description of any benefits to the subject or to others that 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 must be maintained;

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;

7. An explanation of whom to contact on the research team for questions about the research, concerns or complaints about the research, and whom to contact in the event of a research-related injury to the subject;
8. Contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research;
9. Contact information for someone independent of the research team for problems, concerns or complaints;
10. 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;
11. For research subject to the 2018 Common Rule. 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. For FDA-regulated studies, a statement that notes the possibility that the Food and Drug Administration may inspect the records;
13. For "applicable" FDA-regulated clinical trials, the following statement must be included verbatim: "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 Website at any time.

    "Applicable clinical trials are:

    (1) clinical trials of drug and biological products that are controlled, clinical investigations other than Phase I investigations, of a product subject to FDA regulation; and

    (2) prospective clinical studies of health outcomes comparing an intervention with a device product against a control in humans (other than small feasibility studies) or any pediatric post-market surveillance studies required by FDA under the FD&C Act.

14.5 Additional elements of informed consent to be applied, as appropriate:

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) that are currently unforeseeable;

2. 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;

3. Any additional costs to the subject that may result from participation in the research;

4. When applicable, the amount and schedule of all payments;

5. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

6. 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;

7. The approximate number of subjects involved in the study.

8. For research subject to the revise Common Rule (2018 requirements):

    a. 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.

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

    c. 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.

14.7 Subject Withdrawal or Termination

A subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research plans and consent documents.
When seeking informed consent from subjects, the following information regarding data retention and use must be included:

1. For FDA-regulated clinical trials: When a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. This should be disclosed in the consent; or

2. For research not subject to FDA regulations: The investigator should inform subjects whether the investigator or study sponsor intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator or study sponsor will destroy the subject's data or that the investigator or study sponsor will exclude the subject's data from any analysis.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigators should ask a subject who is withdrawing whether the subject wishes to participate in continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review. If a subject withdraws from the interventional portion of the study but agrees to continued follow-up as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original consent document). IRB approval of consent documents for these purposes would be required.
If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator must not access or gather private information about the subject for purposes related to the study. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

14.8 Documentation of Informed Consent

Except as provided in Sections 14.10, 14.11 and 14.12 of this manual, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) and dated by the subject or the subject's legally authorized representative at the time of consent. The person obtaining consent will also sign the consent form for greater than minimal risk studies.

2. For research conducted in accordance with ICH-GCP E6 or in facilities subject to Joint Commission requirements, the name of the person who obtained consent and the date they did so is documented on the written consent form

3. A written copy of the signed and dated consent form must be given to the person signing the form. The investigator should retain the signed original in the research records and place a copy in the facility medical record.

The consent form may be either of the following:

1. For research subject to the FDA or DOJ regulations: A written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the subject or the subject's legally authorized representative, but the

subject or representative must be given adequate opportunity to read it before it is signed; or

2. For research subject to the 2018 Common Rule requirements: A written consent document that embodies the basic and required additional elements of informed consent. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's LAR; or

3. A short form written informed consent form stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative (LAR), and, for research subject to the 2018 Common Rule, the key information required (see 'General Requirements' above) was presented to the subject first, before other information if any, was provided The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative.

   When this method is used:

   a. The oral presentation and the short form written document should be in a language understandable to the subject; and

   b. There must be a witness to the oral presentation; and

   c. The IRB must approve a written summary of what is to be said to the subject (the approved full consent document may serve as this summary); and

   d. The short form document is signed by the subject or legally authorized representative;

   e. The witness must sign both the short form and a copy of the summary; and

   f. The person actually obtaining consent must sign a copy of the summary; and

   g. A copy of the summary must be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.

When this procedure is used with subjects who do not speak, or read, English, or have limited proficiency in oral or written English, (i) the oral presentation and the short form written document should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject. When the person obtaining consent is assisted by an interpreter, the interpreter may serve as the witness.

The IRB must receive all foreign language versions of the short form document as a condition of approval. Expedited review of these versions is acceptable if the protocol/research plan, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB.

14.9 Special Consent Circumstances

14.9.1 Electronic Informed Consent (eIC)

The ethical obligation to obtain informed consent for participation in research is fundamental; however, U.S. regulations do not specify a particular method for the informed consent process. Recognizing the increased interest in using electronic informed consent (eIC) to replace or supplement the traditional paper-based process, OHRP and FDA issued joint guidance on the topic in 2016. Per the guidance, eIC refers to *"the use of electronic systems and processes that may employ multiple electronic media, including text, graphics, audio, video, podcasts, passive and interactive Web sites, biological recognition devices, and card readers, to convey information related to the study and to obtain and document informed consent."* Investigators planning to use eIC should review the guidance in advance to ensure that the eIC process and platform meet OHRP and FDA (as applicable) expectations.

Investigators proposing to use eIC should submit copies of all forms and informational materials (e.g., video content, hyperlinked webpages) that the potential subject will review during the eIC process. If the eIC includes questions or other methods to gauge subject comprehension, these should also be provided. Investigators are responsible for periodically reviewing any linked to materials to ensure that the content remains available and is unchanged. Any changes to the eIC or any of the supplemental information must be submitted to the IRB for review and approval.

Whether the eIC process takes place in person or remotely, the responsibility for obtaining informed consent remains with the investigator and any appropriately delegated study team members. When the eIC process takes place remotely and is not witnessed by the investigator or study team members, the eIC generally should include a method to ensure that the person electronically signing the eIC is the subject or their LAR, when applicable. Exceptions to this general rule may be acceptable in certain circumstances (e.g., minimal risk research).
As with any other form of consent, the eIC process must allow for sufficient time for the potential subject to consider whether to participate and must include a mechanism for potential subjects to ask questions and have them answered. A copy of the eIC must be provided to participants, including copies of any supplemental materials. The copy provided to participants may be hardcopy or electronic.

Electronic signatures must be compliant with applicable legal requirements, including those of the jurisdiction where the research is to be conducted, and the FDA's requirements, when applicable.

14.9.2 Enrollment of persons with limited English-language proficiency

1. **Expected enrollment**: In some studies, the investigator may be able to anticipate enrollment of persons who do not speak or read, or have limited proficiency in, oral or written English. When the target subject population includes such persons or the investigator and/or the IRB otherwise anticipates that consent will be conducted in a

language other than English, the IRB requires a translated consent document, and other subject materials, to be prepared. In order to ensure that translated documents are accurate, the IRB may choose to require a certified translation, to have an independent back-translation or to have a review of the translated documents by an IRB member or other person who is fluent in that language. When non-English speaking subjects enroll, they and a witness sign the translated consent document. The subjects are given a copy of the translated consent document.

2. Unexpected enrollment: If a person who does not speak or read, or has limited proficiency in, English presents for possible enrollment, an IRB- approved translated version of the written consent may not be available for use. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented during the consent process or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.

   If an investigator decides to enroll a subject into a study for which there is not an extant IRB-approved consent document in the prospective subject's language, the investigator must receive IRB approval to follow the procedures for a "short form" written consent.

3. 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 facilitate the consent discussion. Preferably someone who is independent of the subject (i.e., not a family member) should assist in presenting information and obtaining consent. Whenever possible, interpreters should be provided copies of the translated consent, or short form and the IRB-approved consent script (typically the English-language version of the consent document) well before (24 to 48 hours if possible) the consent discussion with the subject. If the interpreter also serves as the witness, she/he may sign the translated consent, or short form consent document and script, as the witness and should note "Interpreter" under the signature line. The person obtaining consent must document that the "short form" process was used in the subject's research record, including the name of the interpreter.

14.9.3 Braille Consent

For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure itself that a Braille consent document is accurate; the IRB may require a transcription into print text or review of the document by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise, oral consent will be obtained, witnessed and documented as described under "Oral Consent".

14.9.4 Oral Consent

When subjects are unable to read a written consent form (such as blind or illiterate subjects), the IRB may approve an oral consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained orally and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria described below when IRB approved.

For greater than minimal risk research, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may also be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide oral consent. The person obtaining consent and a witness will sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave oral consent. The consent process will also be documented in the subject's research record. Signed copies of the consent form are given to the subject and, whenever possible, these documents should be provided to the subject on audio or videotape.

14.9.5 Physically Challenged Subjects

A person who is physically challenged (e.g., physically unable to talk or write) can enroll in research if competent and able to indicate voluntary consent to participate. Whenever possible, the subjects should sign the consent form or make their mark by initialing or making an X. As with oral consent, a witness to the consent process is recommended and the circumstances and consent process should be carefully documented in the research records.

14.10 Waiver or Alteration of Informed Consent

General Waiver or Alteration

<u>For research subject to FDA or DOJ regulations:</u>

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

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 or legally authorized representatives will be provided with additional pertinent information after participation.

<u>For research subject to the 2018 Common Rule:</u>

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration"), provided that the IRB finds and documents that the below criteria are satisfied.

1. The research or clinical investigation involves no more than minimal risk to the

subjects;

2. The research or clinical investigation could not practicably be carried out without requested waiver or alteration;

3. 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;

4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

5. Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

Public Benefit or Service Programs Waiver or Alterations

For research subject to DOJ regulations: (Note: this option is not available to research subject to FDA regulations) In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements 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:
    a. Public benefit or service programs;
    b. Procedures for obtaining benefits or services under those programs;
    c. Possible changes in or alternatives to those programs or procedures; or
    d. 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.

For research subject to the 2018 Common Rule: An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied. Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration"), provided that the IRB finds and documents that the below criteria are satisfied.

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:
    a. Public benefit or service programs;

b. Procedures for obtaining benefits or services under those programs;

c. Possible changes in or alternatives to those programs or procedures; or

d. 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.

14.10.1 Screening, Recruiting, or Determining Eligibility

For research subject to the Common Rule: An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

3. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

Note: The provisions described in this section do not apply to DOJ-regulated research. These provisions do not appear in FDA regulations; however, the FDA does not consider records review or oral communication with potential subjects prior to obtaining consent to be part of a clinical investigation, therefore waivers are not required. See FDA Draft Guidance for more information.

14.11 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

1. The only record linking the subject and the research would be the informed consent form, and the principal risk would be potential harm resulting from a breach of confidentiality; Each subject (or LAR) must be asked whether they want documentation linking them with the research, and their wishes must govern. (Example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to investigators.)

   This option does not apply to FDA-regulated research.

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 of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews

generally do not require written consent when conducted by non-investigators (e.g., marketing surveys, telemarketing)

The FDA does permit a waiver of documentation of consent if this condition is satisfied. This is most commonly applied in the context of minimal risk screening activities that are necessary to determine eligibility for enrollment in the full trial;

Or

3. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

   This option does not apply to research subject to the pre-2018 Common Rule or to FDA or DOH regulations.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an adequate consent process.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

14.12 Waiver of Informed Consent for Planned Emergency Research

The conduct of planned research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived by the IRB is covered by 21 CFR §50.24 for FDA-regulated research and by the waiver articulated by HHS at 61 FR 51531-33 for non-FDA-regulated research.

The FDA exception from informed consent requirements for emergency research under FDA regulations, 21 CFR 50.24, permits planned research in an emergency setting when human subjects who are in need of emergency medical intervention, cannot provide legally effective informed consent themselves, and there is generally insufficient time and opportunity to locate and obtain consent from their legally authorized representatives (LARs).

The Secretary of Health and Human Services (HHS) has implemented an Emergency Research Consent Waiver under 45 CFR 46.101(i) with provisions equivalent to those of the FDA with the exception of the requirements specified below. The HHS waiver is not applicable to research involving prisoners, pregnant women, fetuses, or in vitro fertilization.

14.12.1 Definitions

Family Member: For this section, a family member is any one of the following adult and 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.
Planned Emergency Research: research that involves subjects who are in a life-threatening situation for which available therapies or diagnostics are unproven or unsatisfactory, and because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, it is generally not possible to obtain legally effective informed consent.

14.12.2 Procedures

The IRB may approve the planned emergency research without requiring informed consent of all research subjects prior to initiating the research intervention if the IRB finds and documents that the following conditions have been met:

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:
    a. The subjects will not be able to give their informed consent as a result of their medical condition;
    b. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
    c. 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:
    a. Subjects are facing a life-threatening situation that necessitates intervention;
    b. 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
    c. 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 plan 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 legally authorized 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 consistent with Sections 46.116 and 46.117 of 45 CFR 46 and Sections 50.20, 50.25 and 50.27 of 21 CFR 50. 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 E of this section.

7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:

    a. 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;

    b. 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 clinical investigation, of plans for the investigation and its risks and expected benefits;

    c. Public disclosure of sufficient information following completion of the research to apprise the community and investigators of the study, including the demographic characteristics of the research population, and its results;

    d. Establishment of an independent data monitoring committee to exercise oversight of the research; and

    e. 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.

14.12.2.1 FDA-regulated Planned Emergency Research

A licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation must concur that the conditions described above are satisfied.

Studies involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that such studies may include subjects who are unable to consent. The submission of those studies in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided in the regulations or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the

clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.
The IRB determinations and documentation required are to be retained by the IRB in accordance with HRPP 1210.

14.12.2.2 Planned Emergency 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 found and documented that the research is not subject to regulations codified by the FDA at 21 CFR Part 50 and has found and documented and reported to the OHRP that the conditions required have been met relative to the research.

14.13 Posting of Clinical Trial Consent

For each clinical trial conducted or supported by a federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal

Web site that will be established as a repository for such informed consent forms.

If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

15 Vulnerable Subjects in Research

When some or all of the participants in a research study conducted by the affiliates of Baptist are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these participants. The IRB must ensure that all of the regulatory requirements for the protection of vulnerable subjects are met and that appropriate additional protections for vulnerable subjects are in place.

The following procedures describe the requirements for involving vulnerable participants in research under the auspices of Baptist.

15.1 Definitions

Children: Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. See Section 1.11.13 for definitions of a minor for the states in which Baptist most often conducts human subject research. NOTE: For research conducted in jurisdictions other than Tennessee, Mississippi or Arkansas, the research must comply with the laws regarding the legal age of consent in the relevant jurisdictions. Baptist's Legal counsel will be consulted with regard to the laws in other jurisdictions.

Dead fetus: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

Delivery: A delivery is a complete separation of the fetus from the woman by expulsion or extraction or any other means.

Fetus: A fetus means the product of conception from implantation until delivery.

Guardian: A guardian is an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. NOTE: For research conducted in jurisdictions other than Tennessee, the research must comply with the laws regarding guardianship in all relevant jurisdictions. Baptist's Legal counsel will be consulted with regard to the laws in other jurisdictions.

Neonate: A neonate is a newborn.

Nonviable neonate: A nonviable neonate means a neonate after delivery that, although living, is not viable.

Pregnancy: A pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

Prisoner: A prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment

procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Viable: As it pertains to the neonate, viable means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a neonate is viable, then, for the purposes of participation in research, the neonate is considered a child and the rules regarding participation of children in research apply.

Ward: A ward is a child placed under the protection of a legal guardian by the State or any other authorized agency or institution.

15.2 Involvement of Vulnerable Populations

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process should include one or more individuals who are knowledgeable about and experienced in working with these participants. When the IRB does not have the relevant expertise among its membership, expertise may be sought through the use of consultants.

The regulations to protect human subjects in research at 45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations which also have additional requirements for IRBs:

1. Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
2. Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
3. Subpart D - Additional Protections for Children Involved as Subjects in Research

Non-exempt HHS-conducted or supported research that involves any of these populations must comply with the requirements of the relevant subparts. Research regulated by the FDA includes equivalent protections and obligations when research involves children (Subpart D). Research conducted, supported, or otherwise regulated by other federal departments or agencies may or may not be covered by the subparts.

In its FWA, Baptist limits its commitment to apply Subparts B, C, and D to non- exempt human subject research conducted or supported by HHS or any other federal agency that requires compliance with the Subpart(s) (B, C, or D) applicable to the research.

The following policies and procedures, which are based on Subparts B, C, and D, apply to all research regardless of funding. The individual sections describe how the subparts apply specifically to HHS-funded research.

15.2.1 Responsibilities

- The investigator is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal, including the possible inclusion of subjects who

are at risk for impaired decisional capacity, and who are being asked to participate in a research study with greater than minimal risk.

- The IRB shall include representation, either as members or through the use of consultants, of individual(s) who are knowledgeable about or experienced working with the vulnerable populations involved in the research proposal under review.
- The IRB reviews the investigator's justifications for including vulnerable populations in the research to assess appropriateness for inclusion in the research proposal.
- The IRB must ensure that appropriate additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects at the time of initial review of the research proposal.
- Information reviewed as part of the continuing review process should include the number of participants considered to be members of specific vulnerable populations

15.3 Procedures:

The following policies and procedures apply to all research involving vulnerable populations *(subjects vulnerable to coercion or undue influence)* under the oversight of the Baptist IRB regardless of funding. Subsequent sections address additional procedures and requirements that apply to specific populations.

Initial Review of Research Proposal

1. The investigator identifies the potential to enroll vulnerable subjects in the proposed research at initial review and provides the justification for their inclusion in the study.
2. The investigator describes safeguards to protect the subject's rights and welfare in the research proposal.
3. The IRB, with relevant expertise with the vulnerable population in question, evaluates the proposed safeguards, including, if applicable, the proposed plan for obtaining consent from legally authorized representatives and the plans for assent of children and adults unable to provide consent. The IRB further evaluates:
    a. whether inclusion of vulnerable populations is ethically and scientifically appropriate;
    b. whether the proposed plans, including the settings and circumstances, for identification and recruitment of subjects, and for obtaining consent or parental permission, ensure equitable selection of subjects and promote voluntariness;
    c. Whether the proposed research confers any direct benefit, whether the benefit is available outside of the research, and whether access to the benefit may unduly influence participation by vulnerable populations;
    d. Whether any costs or plans for subject reimbursement or compensation may exclude or unduly influence participation by vulnerable populations;

e. Whether the provisions for privacy and confidentiality adequately protect vulnerable populations; and
f. Other relevant considerations as appropriate for the population(s) and the circumstances of the research

4. The IRB will determine whether the inclusion of the vulnerable population(s) is appropriate and whether the proposed plan adequately safeguards the rights and welfare of these subjects. When appropriate, the IRB may restrict or disallow the inclusion of vulnerable subjects or may require modifications to the research plan to enhance protections or to monitor the effectiveness of protections. For example, the IRB could require review more than annually, periodic HRPP QA/QI reviews, independent routine monitoring, or the use of a data and safety monitoring board, consent monitor, or research subject advocate or consent monitor.

Modifications to Research

1. When an investigator proposes to add inclusion of a vulnerable population after research has already been approved by the IRB, the investigator must submit a modification request to the IRB identifying the population they would like to add, justification for inclusion of the population, and any modifications to the research plan to ensure protection of the subjects' rights and welfare;

2. The IRB staff and IRB will follow the procedures outlined for initial review above;

Continuing Review

1. At continuing review the investigator should identify the number and categories of vulnerable subjects enrolled and any problems that arose relevant to their rights and welfare. When research does not include any interaction or intervention with subjects, and such information is not gathered, this should be noted on the continuing review report;

2. IRB staff, in collaboration with the IRB Chair as needed, ensure that the IRB has the relevant expertise with the vulnerable population, and, if necessary, arrange for consultation. When the research involves no more that minimal risk and is eligible for expedited review, the designated reviewer may determine the need for additional expertise to ensure the protection of the vulnerable population(s);

3. The IRB reviews the continuing review information, and any relevant information reported to the IRB during the period of approval and determines whether the inclusion of vulnerable populations and the plans to protect the rights and welfare of vulnerable subjects remains appropriate.

15.4 Research Involving Pregnant Women, Fetuses and Neonates

The following applies to all research regardless of funding source. For research not conducted or supported by HHS, where the risk to the pregnant women and fetus is no more than minimal, no additional safeguards are required by policy and there are no restrictions on the involvement of

pregnant women in research. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

If a woman becomes pregnant while participating in a study that has not been approved for inclusion of pregnant women, the IRB must be notified immediately so that the IRB can determine whether the subject may continue in the research, whether additional safeguards are needed, and to make the determinations required by the regulations and these policies.

15.4.1 Research Not Conducted or Supported by DHHS

For research not conducted or supported by DHHS, where the risk to the pregnant women and fetus is no more than minimal, no additional safeguards are required by policy and there are no restrictions on the involvement of pregnant women in research. However, the IRB may determine that additional safeguards or restrictions are warranted for a specific study.

Pregnant women or fetuses may be involved in research not funded by DHHS **involving more than minimal risk** to pregnant women and/or fetuses if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

3. Any risk is the least possible for achieving the objectives of the research;

4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.

5. If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

7. For children (as defined in Definitions) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section IX.C.2.;

8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

10. Individuals engaged in the research will have no part in determining the viability of a neonate.

Research specifically designed to study fetuses will not be conducted at Baptist.

Research involving nonviable neonates or neonates of uncertain viability will not be conducted at Baptist.

Research involving elective abortions, stem cells taken from fetuses, gender reassignment or other similar transgender therapies will not be conducted at Baptist.

Viable Neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements for Research Involving Children (i.e., a viable neonate is a child for purposes of applying federal regulations and Baptist policies).

15.4.2 Research Conducted or Supported by DHHS

For DHHS-conducted or supported research, 45 CFR Subpart B applies to all non-exempt human subject research involving pregnant women, fetuses, and neonates.

Pregnant women or fetuses may be involved in research if all the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses.
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect

of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent.

5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children (as defined in Section 15.1) who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 15.6.2;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

Research specifically designed to study fetuses will not be conducted at Baptist.

Research involving nonviable neonates or neonates of uncertain viability will not be conducted at Baptist.

Research involving elective abortions, stem cells taken from fetuses, gender reassignment or other similar transgender therapies will not be conducted at Baptist.

Viable Neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements for Research Involving Children (i.e., a viable neonate is a child for purposes of applying federal regulations and Baptist policies).

15.4.3 Research Not Otherwise Approvable

For research not conducted or supported by HHS, if the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either that the research in fact satisfies the conditions detailed above, as applicable; or the following:

1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;

2. The research will be conducted in accord with sound ethical principles; and

3. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

4. For research conducted or supported by HHS, if the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for HHS review.

15.5 Research Involving Prisoners

This policy applies to all biomedical and behavioral research conducted under the auspices of Baptist involving prisoners as subjects. Even though the IRB may approve a research study involving prisoners as subjects according to this policy, investigators are still subject to the Administrative Regulations of the Department of Corrections and any other applicable State or local law. [45 CFR 46.301]

Prisoners are not a population of study at Baptist. If an enrolled participant becomes incarcerated during the course of a study, the IRB will consider and adopt policies consistent with Subpart C of 45 CFR 46.

15.5.1 Incarceration of Enrolled Subjects

If a participant becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C, the investigator must promptly notify the IRB and the IRB shall:

1. Confirm that the participant meets the definition of a prisoner;

2. Consult with the investigator to determine if it is in the best interests of the participant to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject and should continue until the IRB is able to review the research study under Subpart C;

If the participant should continue, one of two options are available:

1. Keep the participant enrolled in the study and review the research under Subpart C. If some of the requirements of Subpart C cannot be met or are not applicable (e.g., procedures for the selection of subjects within the prison), but it is in the best interests of the participant to remain in the study, keep the participant enrolled and inform OHRP of the decision along with the justification; or

2. Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.

If a participant is incarcerated temporarily while enrolled in a study:

1. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities to take place during the temporary incarceration), keep the participant enrolled; or

2. If the temporary incarceration has an effect on the study, follow the above guidance.

15.5.2 Certification to HHS

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is conducted or supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving a researchsubject who becomes incarcerated. Certifications, and requests for HHS Secretarial consultation, do not need to be submitted to OHRP for research not conducted or supported by HHS, regardless of whether the institution has chosen to extend the applicability of its FWA and Subparts B, C, and D to all research.

For all HHS conducted or supported research, Baptist will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research study in question and any relevant HHS grant application or protocol/research plan. HHS conducted or supported research involving subjects who have become incarcerated may not proceed until OHRP issues its authorization in writing to Baptist on behalf of the Secretary under 45 CFR 46.306(a)(2).

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submits to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes:

- The IRB-approved protocol/research plan; any relevant HHS grant application or proposal;
- Any IRB application forms required by the IRB;
- And any other information requested or required by the IRB to be considered during initial IRB review.

OHRP also encourages the organization to include the following information in its prisoner research certification letter to facilitate processing:

- The OHRP Federalwide Assurance (FWA) number;
- The IRB registration number for the designated IRB; and
- The date(s) of IRB meeting(s) in which the study was considered, including a brief

chronology that encompasses:

- The date of initial IRB review; and
- The date of subpart C review, if not done at the time of initial IRB review.

15.5.3 Waiver for Epidemiology Research

The HHS Secretarial waiver for certain epidemiological research conducted or supported by HHS functions as a fifth category of permissible research [68 FR 36929]. The criteria for this category are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.

The organization still must review the research under subpart C and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings under HHS regulations at 45 CFR 46.305(a) and receive OHRP authorization prior to initiating any research involving a research subject who has become incarcerated. All of the other requirements of subpart C apply to research in this category.

15.6 Research Involving Children

The following applies to all research involving children and the requirements in this section are consistent with Subpart D of 45 CFR 46 which applies to HHS conducted or funded research and Subpart D of 21 CFR 50, which applies to FDA-regulated research involving children.

15.6.1 Allowable Categories

In addition to the IRB's normal duties, research involving children must be reviewed by the IRB to determine if it fits within and is permissible under one or more federally defined categories (OHRP/FDA). Each procedure or intervention that the child will undergo for the research must be taken into consideration, and, if the research includes more than one study group assignment (e.g., placebo vs. active, investigational agent vs. comparator) the category determination must be made for each group assignment. In other words, a component analysis must be conducted by the IRB. The categories are as follows:

[45 CFR 46.404/21 CFR 50.51] Research/Clinical Investigations not involving greater than minimal risk. Research determined to not involve greater than minimal risk to child subjects may be approved by the IRB only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in Section 15.6.2.

[45 CFR 46.405/21 CFR 50.52] Research/Clinical Investigations involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may be approved by the IRB only if the IRB finds and documents that:

a. The risk is justified by the anticipated benefit to the subjects;

b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative options; and

c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 15.6.2.

[45 CFR 46.406/21 CFR 50.53] Research/Clinical Investigations involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition. Research in which the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, may be approved by the IRB only if the IRB finds and documents that:

a. The risk represents a minor increase over minimal risk;

b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

d. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 15.6.2.

[45 CFR 46.407/21 CFR 50.54] Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children. When the IRB does not believe that the research meets the requirements of any of the above categories, and the IRB finds and documents that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, the IRB shall refer the research for further review as follows:

- HHS conducted or supported research in this category will be referred for review by the Secretary of Health and Human Services. However, before doing so the IRB must determine that the proposed research also meets all the requirements of the Common Rule.

- FDA-regulated research in this category will be referred for review by the Commissioner of Food and Drugs.

- For research that is not HHS conducted or supported and not FDA- regulated, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either that the research in fact

satisfies the conditions of the previous categories, as applicable; or the following:

- The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- The research will be conducted in accord with sound ethical principles; and
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 15.6.2.

15.6.2 Parental Permission and Assent

15.6.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian. Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 14.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 [45 CFR 46.404/21 CFR 50.51] & 2 [45 CFR 46.405/21 CFR 50.52] above. The IRB's determination of whether permission must be obtained from one or both parents will be documented in the reviewer's notes when a study receives expedited review, and in meeting minutes when reviewed by the convened committee.

Permission from both parents is required for research to be conducted under Categories 3 [45 CFR 46.406/21 CFR 50.53] & 4 [45 CFR 46.407/21 CFR 50.54] above unless:

1. One parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one parent has legal responsibility for the care and custody of the child.

For research not covered by the FDA regulation, the IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

1. The research meets the provisions for waiver in Section 14.10; or
2. For research that is not FDA-regulated, i the IRB determines that the research is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children) provided that an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with 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/research plan, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 14.

15.6.2.2 Assent from Children

The IRB is responsible for determining that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. This judgment may be made for all children to be involved in the study, or for each child, as the IRB deems appropriate.

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for research that meets the provisions for a general waiver in Section 14.10.

Because "assent" means a child's affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way.

The IRB should take into account the nature of the proposed research activity and the ages, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity, but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

Parents and children will not always agree on whether the child should participate in research. Where the IRB has indicated that the assent of the child is required in order for him or her to be enrolled in the study, dissent from the child overrides permission from a parent. Similarly, a child typically cannot decide to be in research over the objections of a parent. There are individual exceptions to these guidelines but in general, children should not be forced to be research subjects, even when permission has been given by their parents.

15.6.2.3 Documentation of Assent

When the IRB determines that assent is required, it also is also responsible for determining whether and how assent must be documented. When the research targets the very young child or children unable or with limited capacity to read or write, an oral presentation accompanied perhaps by some pictures with documentation of assent by the person obtaining assent in a research note is likely more appropriate than providing the child a form to sign. In this case, the investigator should provide the IRB with a proposed script and any materials that they intend to use in explaining the research.

When the research targets children who are likely able to read and write, investigators should propose a process and form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should describe:

1. why the research is being conducted;
2. what will happen and for how long or how often;
3. that it is up to the child to participate and that it is okay to say no;
4. if it will hurt and if so for how long and how often;
5. what the child's other choices are;
6. any good things that might happen;
7. whether there is any compensation for participating; and
8. Ask for questions.

Whenever possible, the document should be limited to one page. Illustrations might be helpful, and larger type and other age appropriate improvements are encouraged when they have the potential to enhance comprehension. Studies involving older children or adolescents should include more information and may use more complex language.

15.6.3 Wards

Although Baptist does not generally conduct studies involving children who are wards, in certain circumstances the following may apply; Children who are wards of the State or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406/21 CFR 50.53 or 45 CFR 46.407/21 CFR 50.54, only if such research is:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research meets the condition(s) above, an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in *loco parentis.*

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

15.7 Adults with Impaired Decision Making Capacity

When vulnerable populations are included in research, regulations require that additional safeguards are put in place to protect the rights and welfare of these subjects. [45 CFR 46.111(b)/21 CFR 56.111(b)] Adults who lack or who have impaired, fluctuating, or diminishing decision-making capacity (collectively referred to as "adults with impaired decision-making capacity" in this section) are particularly vulnerable. Investigators and IRBs must carefully consider whether inclusion of such subjects in a research study is appropriate; and when it is, must consider how best to ensure that these subjects are adequately protected. The principals and procedures outlined in this section are intended to assist Baptist investigators and the IRB with the development and review of research involving adults with impaired decision-making capacity.

15.7.1 Informed Consent

Obtaining legally effective informed consent before involving human subjects in research is one of the central ethical principles described in the Belmont Report and provided for by federal regulations governing research.

As discussed previously, the informed consent process involves three key features: (1) providing the prospective subject the information needed to make an informed decision (in language understandable to him or her); (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether to participate in the research.

Among other requirements, for consent to be legally effective, the potential subject or their LAR must have the necessary decision-making capacity to make a rational and meaningful choice about whether to participate (or continue participating) in a study.

15.7.2 Decision-Making Capacity

"Decision-making capacity" refers to a potential subject's ability to make a rationale and meaningful decision about whether or not to participate in a research study. This ability is generally thought to include at least the following four elements:

1. Understanding, i.e., the ability to comprehend the disclosed information about the nature and purpose of the study, the procedures involved, the risks and benefits of participating versus not participating, and the voluntary nature of participating;

2. Appreciation, i.e., the ability to appreciate the significance of the disclosed

information and the potential risks and benefits for one's own situation and condition;

3. Reasoning, i.e., the ability to engage in a reasoning process about the risks and benefits of participating versus alternatives, and;

4. Choice, i.e., the ability to express a choice about whether or not to participate.

"Decision-making capacity" should not be confused with the legal concept of "competence." While the court may consider information about a person's decision-making capacity in making a competency determination, the terms are not synonymous. Incompetence is a legal determination made by a court of law. For example, someone who is judged legally incompetent to manage their financial affairs may retain sufficient decision-making capacity to make meaningful decisions about participating in a research protocol. Likewise, people who have normal cognitive functioning and are considered legally competent may be put into circumstances where their decision-making capacity is temporarily impaired by a physical or mental condition or by alcohol or drugs.

Decision-making capacity is protocol and situation specific. A person may have capacity to consent to participate in low risk research in usual circumstances but not have the capacity to consent to a higher risk protocol when s/he is under significant stress or faced with unfamiliar circumstances.

15.7.3 Inclusion of Adults with Impaired Decision-Making Capacity in Research

Research involving adult subjects without the ability to provide consent or with impaired decision-making capacity should only be conducted when the aims of the research cannot reasonably be achieved without their participation.

Investigators must disclose to the IRB both plans and justification for including adults with impaired decision-making capacity in a given research proposal. If adults with questionable or fluctuating capacity will be included, investigators must specify procedures for assessing capacity prior to providing informed consent and, if appropriate, for re-evaluating capacity during study participation. If a prospective subject's capacity to consent is expected to diminish, the investigator should consider requesting that the subject designate a future LAR prior to enrollment in the research, including the future LAR in the initial consent process, and obtaining written documentation of the subject's wishes regarding participation in the research. When the study includes subjects likely to regain capacity to consent while the research is ongoing, the investigator should include provisions to inform them of their participation and seek consent for ongoing participation.

Plans for evaluation of capacity should be tailored to the subject population and the risks and nature of the research. In some instances, assessment by a qualified investigator may be appropriate. However, an independent, qualified assessor should evaluate subjects' capacity when the risks of the research are more than a minor increase over minimal or the investigator is in a position of authority over a prospective subject. In all cases, the person(s) evaluating capacity must be qualified to do so and use appropriate, validated tools and methods (e.g., University of California, San Diego Brief Assessment of Capacity to

Consent [UBACC], MacArthur Competence Assessment Tool for Clinical Research [MacCAT-CR]). Assessments of capacity should be documented in the research record, and when appropriate, in the medical record.

Under some circumstances, it may be possible for investigators to enable adults with a degree of decisional impairment to make voluntary and informed decisions to consent, assent, or refuse participation in research. Potential measures include repetitive teaching, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent discussions, use of waiting periods to allow more time for the potential subject to consider the information that has been presented, or involvement of a trusted family member or friend in the disclosure and decision-making process. Audio or videotapes, electronic presentations, or written materials used to promote understanding must be provided to the IRB for review and approval prior to use.

When a prospective subject is deemed to lack capacity to consent to participate in research, investigators may obtain informed consent from the individuals' surrogate or LAR. Under these circumstances, the prospective subject should still be informed about the research in a manner compatible with the subjects' likely understanding and, if possible, be asked to assent to participate. Potential subjects who express resistance or dissent (by word, gesture, or action) to either participation or use of surrogate consent, should be excluded from the study. Some subjects may initially assent but later resist participation. Under no circumstances may an investigator or caregiver override a subject's dissent or resistance. When assent is possible for some or all subjects, the investigator should provide the IRB with an assent plan that describes when and how assent will be obtained, provisions that will be taken to promote understanding and voluntariness, how assent will be documented, and a copy of the assent form. If the investigator intends to use audio or video recordings to document assent, provisions to ensure the security of the recordings should be described to the IRB.

When inclusion of adults with impaired decision-making capacity is not anticipated and a plan for inclusion of such subjects has not been reviewed and approved by the IRB, and an enrolled subject becomes unable to provide consent or impaired in decision-making capacity, the investigator is responsible for promptly notifying the IRB (as soon as possible but within 5 business days). The investigator should consider whether continuing participation is appropriate and, if so, present a plan for surrogate consent from a LAR and, if appropriate, a plan to periodically evaluate capacity and re-obtain consent if possible.

15.7.4 IRB Review

The IRB review process will include at least one member, or a consultant, who is experienced with or otherwise knowledgeable about the population when the research involves greater than minimal risk, or the research is minimal risk but includes interactions with subjects, and the proposed subject population includes adults with impaired decision-making capacity.

In evaluating research, the IRB must be able to determine that the risks to subjects are

reasonable not only in relation to any benefits, but also in relation to the importance of the knowledge that may reasonably be expected to result. In considering the risks of research involving subjects unable to provide informed consent or with diminished capacity to do so, the IRB should consider whether any components of the research involve risks that are greater for participants with diminished capacity. For example, the population might experience increased sensitivity or discomfort to certain stimuli or may not be able to verbalize or otherwise demonstrate when they are experiencing discomfort or pain.

As appropriate to the research, the IRB will consider the following in evaluating greater than minimal risk research involving adults unable to consent or with impaired decision-making capacity:

1. Whether the aims of the research cannot reasonably be achieved without inclusion of the population
2. Whether the research is likely to improve the understanding of the condition, disease, or issue affecting the subject population
3. Whether any experimental procedure or interventions have undergone pre-clinical testing or human testing on other populations and whether the data from that testing supports its use in the proposed research
4. Whether the procedures or interventions that the subject will undergo in the research place them at increased risk and if appropriate mechanisms are in place to minimize risks, when possible
5. Whether the data and safety monitoring plan, including any stopping rules, is appropriate given the risks of the research and the vulnerability of the population
6. Whether the procedures for withdrawing individual subjects from the research are appropriate
7. Whether the recruitment procedures, consent process, and any plans for financial compensation support voluntariness and minimize the likelihood of undue influence or coercion
8. Whether the subjects will be exposed to financial or other risks that they might not consider acceptable if they had the capacity to provide consent, and whether appropriate mechanisms have been put into place to minimize these risks
9. Whether the procedures for determining capacity to provide consent, and for evaluating capacity on an ongoing basis, if applicable, are appropriate
10. Whether the procedures for informing subjects who regain capacity about their involvement in the research, and for obtaining consent for on-going participation, if applicable, are appropriate
11. Whether assent should be required when possible, and, if so, if the proposed procedures

to obtain and document assent are appropriate;

12. Whether periodic re-evaluation of capacity and/or periodic re-consent should be required; and

13. Whether a research subject advocate or consent monitor should be required, for some or all subjects

In general, the IRB will only approve research involving subjects unable to provide consent or with impaired decision-making capacity when the aims of the research cannot reasonably be achieved without inclusion of the population, and there are appropriate provisions to: (1) evaluate capacity, (2) obtain consent (and assent if possible), and (3) otherwise protect subjects.

15.8 Reserved

16 FDA-Regulated Research

FDA regulations apply to research that involves a FDA-regulated test article in a clinical investigation involving human subjects as defined by the FDA regulations. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56. If required by organizational policy or a FWA, 45 CFR 46 must also be applied.

Clinical trials with investigational drugs must be conducted according to FDA's IND regulations, 21 CFR Part 312, and other applicable FDA regulations. Use of an investigational device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA's IDE regulations, 21 CFR Part 812, and other applicable FDA regulations.

16.1 Definitions

Biologics: Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other technologies. In general, the term "drugs" includes therapeutic biological products.

Clinical Investigation. Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies. [21 CFR 50.3(c)]

Dietary Supplement: A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains a dietary ingredient. The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients. See Section 201(ff) of the FD&C Act [21 U.S.C. 321(ff)].

Emergency Use: Emergency use is defined as the use of an investigational product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. [21CFR 56.102(d)]

Humanitarian Use Device (HUD): A Humanitarian Use Device is a device intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

IDE: IDE means an investigational device exemption in accordance with 21 CFR 812.

IND: IND means an investigational new drug application in accordance with 21 CFR Part 312.

Investigational Drug: Investigational or experimental drugs are new drugs that have not yet been approved by the FDA or approved drugs that are being studied in a clinical investigation.

Investigational Device: Investigational device means a device (including a transitional device) that is the object of an investigation. Investigation, as it pertains to devices, means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

In Vitro Diagnostic Product (IVD): In vitro diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. [21 CFR 809.3(a)]

LOA: Letter of Authorization means a written statement by the holder or designated agent or representative permitting the FDA to refer to information in the drug master file (DMF) in support of another person's submission.

Non-Significant Risk (NSR) Device: A non-significant risk device is an investigational device that does not meet the definition of a significant risk device.

REMS: Risk Evaluation Mitigation Strategy: The Food and Drug Administration Amendments Act of 2007 (FDAA) gave the FDA the authority to require a Risk Evaluation and Mitigation Strategy (REMS) from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks.

Significant Risk (SR) Device: Significant risk device means an investigational device that:

a. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or

b. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or

c. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
d. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

16.2 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR 56.104(c)]

2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

16.2.1 Procedures:

At initial submission, the investigator must indicate whether the research involves a test article and is a clinical investigation involving human subjects on the application form.

During a pre-review process, the IRB Coordinator will confirm whether FDA regulations are applicable. If FDA regulations apply and the research is not exempt, the IRB Coordinator will indicate on the agenda that the study is FDA-regulated.

If the study involves investigational drugs and is industry sponsored and, if required by the sponsor, the investigator will indicate on the application form that ICH-GCP(E6) compliance is required and provide an affirmation of compliance. Baptist follows ICH-GCP(E6) to the extent it is consistent with FDA regulations. If the study involves investigational drugs and is industry sponsored and the PI has not indicated ICH-GCP(E6) compliance, the IRB will review the study to determine if ICH-GCP(E6) applies and obtain investigator affirmation of compliance, if needed.

16.3 Investigator Responsibilities

1. The investigator holds additional responsibilities when conducting a clinical trial evaluating FDA-regulated drugs, devices, and other articles. These responsibilities include, but are not limited to, the following:

2. The investigator is responsible for ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs (including biological products) or agreement for clinical investigations of medical devices, the investigational plan and other applicable regulations, and any requirements imposed by the IRB or FDA.

3. The investigator is responsible for personally conducting or supervising the investigation. When certain study-related tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

4. The investigator must maintain a list of the appropriately qualified persons to whom significant trial-related duties have been delegated. This list should also describe the

delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., it can refer to an individual's CV on file and/or training conducted by the investigator/sponsor), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

5. The investigator is responsible for protecting the rights, safety, and welfare of subjects under their care during a clinical trial. This responsibility includes:
   a. Informing subjects that the test articles are being used for investigational purposes and ensuring that the requirements relating to obtaining informed consent are met

   b. Providing reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention

   c. Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, or when specialized care is needed)

   d. Adhering to the protocol/research plan so that study subjects are not exposed to unreasonable risks

   e. As appropriate, informing the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and the subject agrees to the primary physician being informed;

6. The investigator is responsible for reading and understanding the information in the investigator brochure or device risk information, including the potential risks and side effects of the drug or device.

7. The investigator is responsible for maintaining adequate and accurate records in accordance with FDA regulations and to making those records available for inspection by the FDA. These records include but are not limited to: correspondence with other investigators, the IRB, the sponsor, monitors, or the FDA; drug and device accountability records; case histories; consent forms; and documentation that consent was obtained prior to any participation in the study. Records must be obtained for a minimum of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such. Other regulations, such as HIPAA, organizational policies, or contractual agreements with sponsors may necessitate retention for a longer period of time. Prior to destroying records, PI's should contact the IRB office for further guidance.

8. The investigator is responsible for controlling drugs, biological products, and devices according to FDA regulations and the Controlled Substances Act, if applicable.

9. The investigator proposing the clinical investigation will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the test article.

a. The investigator is responsible for investigational drug accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability. Such details will be provided in the IRB submission and reviewed by the IRB for acceptability.

b. The investigator may delegate in writing, as part of the IRB submission, the responsibility detailed in 'a' above to the Pharmacy Service.

c. Investigational drugs and devices must be labeled in accordance with federal and state standards.

d. All devices received for a study must be stored in a locked environment under secure control with limited access. When applicable, proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device, and the disposition of remaining devices at the conclusion of the investigation.

10. The investigator is responsible for investigational drug accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability. Such details will be provided in the IRB submission and reviewed by the IRB and the Pharmacy Service for acceptability.

11. The investigator shall furnish all reports required by the sponsor of the research including adverse events, progress reports, safety reports, final reports, and financial disclosure reports.

11. The investigator will permit inspection of research records by the sponsor, sponsor representatives, HRPP and IRB representatives, the FDA, accrediting bodies, and any other agencies or individuals entitled to inspect such records under regulation, organizational policy, or contractual agreement.

16.4 Digital Health

Certain medical and decision support software have been excluded from the definition of medical device under the 21st Century Cures Act and thus are not subject to FDA's regulations. These include exclusions for software functions:

- Intended for administrative support of a health care facility, including the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost- effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow;

- Intended for maintaining or encouraging a healthy lifestyle and unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition;

- Intended to serve as electronic patient records, including patient-provided information, to the extent that such records are intended to transfer, store, convert formats, or display the equivalent of a paper medical chart, so long as:
    - such records were created, stored, transferred, or reviewed by health care professionals, or by individuals working under supervision of such professionals;
    - such records are part of health information technology that is certified under Section 300jj–11(c)(5) of title 42; and
    - such function is not intended to interpret or analyze patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.
- Intended for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results, findings by a health care professional with respect to such data and results, general information about such findings, and general background information about such laboratory test or other device, unless such function is intended to interpret or analyze clinical laboratory test or other device data, results, and findings; and
- Not intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system; and
    - Is intended for the purpose of displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
    - Is intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and
    - Is intended for the purpose of enabling such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.

Additional information regarding the application of these exclusions is available on the FDA website referenced below.

Research involving software excluded from the definition of medical device will be evaluated by the Baptist IRB in accordance with any other applicable regulations (e.g., the Common Rule, HIPAA) and the criteria outlined in this policy.

Other digital health products may be subject to FDA regulations and will be evaluated accordingly. FDA has provided a website listing of Guidance with Digital Health Content to help the regulated community understand FDA's interpretation and application of the regulations and to describe when FDA will practice enforcement discretion in regards to certain requirements such as those for pre-market review and for device reports. Investigators are encouraged to

consult these guidances in advance of their submission to the IRB and to consult directly with the FDA as needed.

16.5 Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/P's)

Generally, research involving HCT/P's regulated as drugs, devices, and/or biologics will require an IND or IDE depending on how the HCT/P is categorized. Because the regulatory and policy framework for HCT/P's is complex, consultation with the FDA prior to submission to the IRB is encouraged to appropriately categorize the HCT/P, understand which regulations and requirements apply, and to obtain an IND or IDE if necessary (or FDA determination that such is not required).

16.6 Dietary Supplements

Research involving dietary supplements may or may not fall under FDA regulations. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body (i.e., not intended to be used for a therapeutic purpose). Whether a study falls under FDA oversight is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body, FDA research regulations do not apply. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, then FDA regulations do apply. Studies involving the ingestion of dietary supplements that are not subject to FDA oversight are still research and therefore must be reviewed by the IRB.

Similarly, whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the study. If the study is intended only to evaluate the dietary supplement's effect on the structure or function of the body, an IND is not required. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.

As with any research involving a test article, the investigator must supply the IRB with sufficient information to determine that the criteria for approval are satisfied and to determine or verify whether or not the research requires an IND. Applications should provide detail consistent with that expected on a drug protocol/research plan and consistent with the level of risk associated or anticipated with the research. At a minimum, the research plan should provide the following information regarding the supplement: Name, Manufacturer, Formulation, Dosage, Method/Route of Administration, Mechanism of Action, Known Drug Interactions, Risk Profile, IND number (or justification for why an IND is unnecessary), documentation of approval for use in humans, documentation or certification of Quality or Purity. As with drugs and devices there should be an accountability plan for the product describing where the product will be stored and how it will be dispensed, usage tracked, and disposal or return. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

16.7 Cannabis and Derivatives

Cannabis and its derivatives, including cannabidiol (CBD), are classified by the FDA as drug products, not as dietary supplements. In most circumstances, research involving the administration of Cannabis and/or its derivatives must be conducted under an IND and comply with FDA's quality requirements. Additional requirements apply when the product is classified as "Marihuana", which is a Schedule 1 controlled substance. Investigators are strongly encouraged to consult with the FDA's Botanical Review Team (BRT) when planning a study involving the use of Cannabis and/or its derivatives to ensure that the study conforms with regulatory requirements and avoid delays in Baptist's review and approval of the research. Investigators are also encouraged to review the information on FDA's website: FDA and Cannabis: Research and Drug Approval Process.

16.8 Clinical Investigations of Drugs and Devices

16.8.1 IND/IDE Requirements

For studies evaluating the safety or effectiveness of medical devices or experiments using drugs, biologics, dietary supplements, and other compounds that may be considered a drug under FDA regulations, the investigator must indicate on the IRB application whether or not an IDE or IND is in place, and, if not, the basis for why an IDE or IND is not needed. Documentation must be provided by the sponsor or the sponsor- investigator. Documentation of the IND/IDE could be a(n):

1. Industry sponsored study with IND/IDE number indicated on the protocol/research plan.
2. Letter/communication from FDA.
3. Letter/communication from industry sponsor.
4. Other document and/or communication verifying the IND/IDE.

For investigational devices, the study may be exempt from IDE requirements or, in the case of Non-Significant Risk (NSR) device studies, follow abbreviated IDE requirements which do not require formal approval by the FDA. If a sponsor has identified a device study as exempt or NSR, then the investigator should include documentation with the submission providing the basis for exempt or NSR categorization. If the FDA has determined that the study is exempt or NSR, documentation of that determination must be provided.

The IRB will review the application and, based upon the documentation provided, determine:

1. that there is an approved IND/IDE in place,
2. that the FDA has determined that an IND is not required or that a device study is exempt or NSR, or,

3. if neither of the above, whether or not an IND is necessary, or that a device study is exempt or NSR, using the criteria below.

The IRB cannot grant approval to the research until the IND/IDE status is determined, and, if necessary, an approved IND or IDE is in place. Note: An IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA.

16.8.2 IND Exemptions

For drugs, an IND is not necessary if the research falls in one of the following seven (7) categories:

1. The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:

    a. The research is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug

    b. In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;

    c. The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

    d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];

    e. The research is conducted in compliance with the requirements of 21 CFR 312.7 (i.e., the research is not intended to promote or commercialize the drug product); and

    f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].

    Please Note: FDA has provided specific guidance for evaluating whether this exemption applies to studies of marketed drugs/biologics for the treatment of cancer.

2. 21 CFR 312.2(b)(2): For clinical investigations involving defined (blood grouping serum, reagent red blood cells, and anti-human globulin) in vitro diagnostic biological products, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 312.160
3. 21 CFR 312.2(b)(5): A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.
4. 21 CFR 320.31(b) and (d): Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:

a. The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;

b. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;

c. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and

d. The sponsor meets the requirements for retention of test article samples [21 CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].

5. 21 CFR 361.1: Research using a radioactive drug or biological product if all of the following conditions are met:

   a. It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;

   b. The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;

   c. The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans, and

   d. The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.

6. FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:

   a. The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;

   b. The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;

   c. The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;

   d. The quality of the cold isotope meets relevant quality standards; and

7. The investigation is conducted in compliance with the requirements for IRB review and informed consent. [21 CFR parts 56 and 50, respectively]

16.8.3 IDE Exemptions

For clinical investigations of devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;

2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a "501k" device);

3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:

    1. Is noninvasive,
    2. Does not require an invasive sampling procedure that presents significant risk,
    3. Does not by design or intention introduce energy into a subject, and
    4. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;

4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

5. The research involves a device intended solely for veterinary use;

6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);

7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

16.8.4 Significant and Non-Significant Risk Device Studies

A device study is a Non-Significant Risk (NSR) Device study if it is not IDE exempt and does not meet the definition of a Significant Risk (SR) Device study.

Under 21 CFR 812.3(m), an SR device means an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

2. Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or

4. Otherwise presents a potential for serious risk to the health, safety, or welfare of

a subject.

If the FDA has already determined a study to be SR or NSR, documentation evidencing such should be provided to the IRB. The FDA's determination is final and the IRB does not have to make the device risk determination.

Unless the FDA has already made a device risk determination for the study, the IRB will review studies that the sponsor or investigator have put forth as NSR at a convened meeting to determine if the device represents SR or NSR.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device).

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's NSR assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, and subject selection criteria.

The NSR/SR determination made by the IRB will be based on the proposed use of the device in the investigation, not on the device alone. The IRB will consider the nature of any harms that may result from use of the device, including potential harms from additional procedures subjects would need to undergo as part of the investigation (e.g., procedures for inserting, implanting, or deploying the device). The IRB may consult with the FDA or require the sponsor or investigator to obtain a determination from the FDA. The IRB will document the SR or NSR determination and the basis for it in the meeting minutes and provide the investigator, and sponsor when applicable, with the determination in writing.

Non-significant risk device studies do not require submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations (21 CFR 812.2(b)). Under the abbreviated requirements, the following categories of investigations are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required:

a. An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):

b. Labels the device in accordance with 812.5;

c. Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;

d. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under Part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).

e. Complies with the requirements of 812.46 with respect to monitoring

investigations;

f. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);

g. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and

h. Complies with the prohibitions in 812.7 against promotion and other practices.

When the FDA or IRB determines that a study is SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained.

16.9 Diagnostic or Treatment Use of Humanitarian Use Devices

A Humanitarian Use Device (HUD) is an approved (marketed) medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year [21 CFR 814.3(n)]. Federal law requires that IRBs approve the use of an HUD at a facility. Once approved, the clinical use of the HUD may be considered as any other approved device, with the caution that effectiveness has not been shown in clinical trials.

16.9.1 Definitions

Humanitarian Device Exemption: A Humanitarian Device Exemption (HDE) is a "premarket approval application" submitted to FDA pursuant to Subpart A, 21 CFR Part 814 "seeking a humanitarian device exemption from the effectiveness requirements of Sections 514 and 515 of the [FD&C Act] as authorized by Section 520(m)(2) of the [FD&C Act]." HDE approval is based upon, among other criteria, a determination by FDA that the HUD will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

HDE Holder: An HDE Holder is a person who or entity that obtains to approval of an HDE from the FDA.

Serious Injury: Serious injury means an injury or illness that:

1. is life-threatening;

2. results in permanent impairment of a bodily function or permanent damage to a body structure; or

3. necessitates medical or surgical intervention to preclude permanent impairment of a bodily function or permanent damage to a body structure (21 CFR 803.3).

16.9.2 IRB Review Requirements

A Humanitarian Use Device (HUD) may only be used in a facility after an IRB has approved its use, except in certain emergencies. The HDE holder is responsible for ensuring that a HUD is provided only to facilities having an IRB constituted and acting in accordance with the FDA's regulations governing IRBs (21 CFR Part 56), including continuing review of use of the device.

When a HUD is used in a clinical investigation (i.e., research involving one or more subjects to determine the safety or effectiveness of the HUD), the full requirements for IRB review and informed consent apply (21 CFR 50 and 56) as well as other applicable regulations. It is essential to differentiate whether the HUD is being studied for the indication(s) in its approved labeling or for different indication(s). When the HUD is being studied for the indication(s) in its approved labeling, the IDE regulations at 21 CFR 812 do not apply. However, when the HUD is being studied for a different indication(s), 21 CFR 812 does apply, including the requirement for a FDA- approved IDE before starting the clinical investigation of a Significant Risk device.

16.9.3 Procedures

The relevant requirements and procedures for investigators and for IRB review described elsewhere in this manual apply to clinical investigations of HUDs. The material within this section applies to diagnostic or treatment uses of HUDs.

The health care provider seeking approval for diagnostic or treatment use of a HUD at Baptist is responsible for obtaining IRB approval prior to use of the HUD at the facility and for complying with the applicable regulations,

including those for medical device reporting, institutional policies, and the requirements of the IRB.

Health care providers seeking initial IRB approval for diagnostic or treatment use of a HUD for the indication(s) in the HUDs approved labeling should submit the following materials to the IRB:

1. Application Form – Humanitarian Use Devices (non-research uses);
2. A copy of the HDE approval letter from the FDA;
3. A description of the device, such as a device brochure;
4. The product labeling;
5. The patient information packet for the HUD;
6. The proposed clinical consent process; and
7. Other relevant materials (e.g., training certificates) as identified in the Application Form

The IRB will review the proposal at a convened meeting ensuring that appropriate expertise is available either within the membership in attendance or via the use of consultants.

The IRB will review the risks to patients that are described in the product labeling and other materials, the proposed procedures to ensure that risks are minimized, and will evaluate whether the risks are reasonable in relation to the potential benefits to patients at the facility.

The IRB will evaluate the patient information packet and proposed consent process and will determine if the materials are adequate and appropriate for the patient population.

The IRB may specify limitations on the use of the device, require additional screening and follow up procedures, require interim reports to the IRB, require continuing review more often than annually, or set other conditions or requirements as appropriate to minimize risks to patients and ensure the safe use of the device in the facility.

Once use of the HUD is approved, the health care provider is responsible for submitting any proposed changes to the IRB-approved plan or patient materials and obtaining approval for those changes prior to implementation, unless the change is necessary to avoid or mediate an apparent immediate risk to a patient. The IRB may review these changes using expedited review procedures or refer the changes for review by the convened IRB.

The health care provider is responsible for submitting reports to the FDA, the IRB, and the manufacturer/HDE Holder whenever a HUD may have caused or contributed to a death, and must submit reports to the manufacturer (or to FDA and the IRB if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)).

The specific requirements for this reporting are in the Medical Device Reporting (MDR) Regulation, at 21 CFR Part 803. The IRB will review these reports via either expedited or convened review, as appropriate, and will consider whether any changes are needed to the IRB-approved plan or patient materials.

The health care provider is responsible for submitting continuing review materials to the IRB sufficiently in advance of the expiration date to ensure IRB review and re-approval prior to expiration. Materials to be submitted include:

1. The Continuing Review Report – Humanitarian Use Devices (non- research uses);
2. Any safety reports or summaries provided by the HDE holder that had not previously been submitted;
3. The current patient information packet, if applicable;
4. The current consent, if applicable;
5. Other materials as identified on the Continuing Review Report;
6. Any other new relevant information or materials;

The IRB may conduct continuing review using expedited review procedures or review by the convened IRB.

16.9.4 Emergency Uses of HUDs

Unapproved HUDs - If an appropriately trained and licensed health care provider in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The health care provider must, within five (5) days after the emergency use of the device, provide written notification of the use to the IRB including the identification of the patient involved, the date of the use, and the reason for the use.

Off-Label Use of HUDs - If a HUD is approved for use in a facility, but an appropriately trained and a licensed health care provider wants to use the HUD outside its approved indication(s) in an emergency or determines that there is no alternative device for a patient's condition, the physician should consult with the HDE holder and IRB in advance if possible, obtain informed consent if possible, and ensure that reasonable measures are taken to protect the well-being of the patient such as a schedule and plan for follow up examinations and procedures to monitor the patient, taking into consideration the patient's specific needs and what is known about the risks and benefits of the device. The provider should submit a follow up report to the HDE holder and the IRB and must comply with medical device reporting requirements.

The IRB may require additional reports, patient protection measures, or other requirement, as appropriate given the specifics of the situation.

16.10 Expanded Access to Investigational Drugs, Biologics, and Devices

Expanded access pathways, also referred to as "compassionate use" for devices, are designed to make investigational medical products available as early in the drug and device evaluation process as possible to patients without therapeutic options, because they have exhausted or are not a good candidate for approved therapies and cannot enter a clinical trial. Expanded access refers to access to investigational medical products outside of a clinical trial, where the intent is treatment, rather than research.

Because the investigational products have not yet been approved by FDA as safe and effective, it is important to remember that the product may not be effective and there may be unexpected serious adverse effects and to take appropriate measures to ensure that this is understood by the patient or their representative and to monitor for safety.

16.10.1 Expanded Access to Investigational Drugs and Biologics

The FDA's expanded access rule for investigational drugs, including biologics classified as drugs, is intended to improve access to investigational drugs for patients with serious or immediately life- threatening diseases or conditions who lack other therapeutic options and may benefit from the investigational agent. Expanded access is sometimes referred to as treatment use.

For the purposes of expanded access to investigational drugs, immediately life-threatening disease or condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early

treatment. Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. [21 CFR 312.300(b)]

Expanded access may also apply to:

1. situations when a drug has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks;

2. use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment during a drug shortage;

3. use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS); and

4. use for other reasons. All are referred to as "investigational" for the purposes of these SOPs.

Under the FDA's expanded access rule, access to investigational drugs for treatment purposes is available to:

1. Individual patients, including in emergencies [21 CFR 312.310]

2. Intermediate-size patient populations [21 CFR 312.315]

3. Widespread use under a treatment protocol or treatment IND [21 CFR 312.320]

The following section addresses expanded access for individual patients. Investigators seeking expanded access for intermediate-size populations or widespread use should consult with the HRPP/IRB office. Convened IRB review is generally required for intermediate or widespread expanded access unless the FDA has issued a waiver.

Physicians seeking access to investigational drugs under expanded access should work closely with the sponsor or manufacturer, the FDA, and the Baptist HRPP, to determine the appropriate access mechanism and ensure that proper regulatory procedures are followed. The FDA provides information about the procedures and requirements for expanded access on a website, including a link to FDA's contact information.

16.10.1.1 Expanded Access to Investigational Drugs for Individual Patients

Expanded access to investigational drugs may be sought under an "Access Protocol" or an "Access IND". FDA generally encourages Access Protocols, which are managed and submitted by the sponsor of an existing IND, because it facilitates the review of safety and other information. However, Access INDs for the treatment of individual patients are

also available and commonly used when:

1. a sponsor holding an existing IND declines to be the sponsor for the individual patient use (e.g., because they prefer that the physician take on the role of sponsor-investigator); or
2. there is no existing IND.

Sponsor or Manufacturer Approval

Prior to submitting to the FDA or IRB, physicians seeking expanded access to an investigational drug should contact the sponsor (e.g., for investigational drugs under a commercial IND) or manufacturer (e.g., for approved drugs under a REMS) to: (1) ensure that the investigational drug can be obtained; (2) determine whether the patient may be treated under an existing IND study, sponsor-held Access Protocol, or if the physician should seek an Access IND; and (3) determine if the drug will be provided free or if there will be a charge. A Letter of Authorization (LOA) from the sponsor or manufacturer should be obtained.

FDA Approval

When a commercial sponsor agrees to provide access under an Access Protocol, the sponsor is responsible for managing and obtaining FDA approval and all other sponsor responsibilities. A licensed physician under whose immediate direction an investigational drug is administered or dispensed for expanded access is considered an "investigator" under FDA regulations and is responsible for all investigator responsibilities under 21 CFR 312, to the extent they are applicable to expanded access.

If the sponsor or manufacturer declines treatment of the patient under an existing IND study or Access Protocol but agrees to make the investigational drug available for the patient, physicians may apply to the FDA for an individual patient Access IND using Form FDA 3926, a streamlined IND application specifically designed for such requests. Form FDA 3926, and related guidance, is available on a FDA website. Form FDA 3926 includes a section where an investigator can request approval from the FDA for alternative IRB review procedures; these alternative procedures enable review by the IRB Chair (or a Chair- designated IRB member) in lieu of review by the convened IRB. This alternative review procedure is referred to as a "concurrence review" in FDA guidance; however, the IRB Chair must review the same materials and make the same determinations as the convened board would. IRB Chair review can also be used for any post-approval reviews (e.g., unanticipated problems, continuing review, closure, etc.).

When there is an emergency situation and insufficient time to submit a written application to the FDA prior to treatment, a request to FDA for emergency use may be made by telephone (or other rapid means). A written expanded access application must be submitted within 15 days of the FDA's authorization.

A physician who obtains an Access IND is considered a "sponsor- investigator" and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 312,

as applicable, including IND safety reports, annual reports, and maintenance of adequate drug accountability records.

IRB Review

Unless the conditions that permit an emergency use exemption are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational drug. When the FDA has authorized the use of alternative IRB review procedures (which can be presumed when the request is made on Form FDA 3926 unless the FDA specifically states that the request is denied), the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using investigational drugs under expanded access should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the drug and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the drug.

To request IRB approval for single patient expanded access, investigators should contact the IRB office and submit the following to the HRPP/IRB Office:

1. A completed Expanded Access Application;
2. A copy of the LOA from the Commercial Sponsor or Manufacturer or other documentation supporting sponsor/manufacturer approval;A copy of the information submitted to the FDA (and FDA approval, if available); A copy of the information submitted to the FDA (and FDA approval, if available);
3. A copy of the Investigator's Brochure or similar documentation that provides information regarding the potential risks and benefits of the investigational drug;
4. A copy of the plan for treating and monitoring the patient; and
5. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but cannot finalize approval until documentation of FDA approval is provided. The IRB will provide the investigator with written documentation of its review.

Baptist will consider reliance upon an external IRB for expanded access when the IND is held by a commercial sponsor and an external IRB has approved the protocol and is willing to accept review and oversight of additionalinvestigators/sites. Investigators should contact the HRPP/IRB office, to discuss IRB reliance for expanded access protocols.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is

necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, copies of any follow-up submissions to the FDA related to the expanded access use must be submitted to the IRB within 7 business days of the date of submission to the FDA.

16.10.1.2 Emergency Use of Investigational Drugs

FDA regulations permit the use of an investigational drug without IRB approval when an appropriately trained and licensed health care provider determines that IRB approval for the use of the drug cannot be obtained in time to prevent serious harm or death to a patient. The provider is expected to assess the potential for benefit from the use of the drug and to have substantial reason to believe that benefits will exist. The criteria and requirements for this Emergency Use Exemption are explained below.

Approval from the FDA and the Sponsor/Manufacturer must be obtained prior to initiating treatment with the drug.

Providers invoking the emergency use exemption must comply with any applicable FDA follow-up requirements including submission of safety reports, amendments, a summary following completion of treatment, and annual reports.

Note: HHS regulations do not permit research activities to be started, even in an emergency, without prior IRB approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject under 45 CFR Part 46. However, nothing in the HHS regulations at 45 CFR Part 46 is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state or local law.

16.10.1.2.1 Emergency Use Exemption from Prospective IRB Approval

Under FDA regulations at 21 CFR 56.104(c), FDA exempts the emergency use of an investigational drug (or biologic classified as a drug) from the requirement for prospective IRB approval, provided that the conditions described below are satisfied and that the emergency use is reported to the IRB within 5 working days. Any subsequent use of the investigational drug in the facility requires IRB approval. However, FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. If it appears likely that the investigational drug may need to be used again, the IRB may request that a study application is submitted which would cover future uses.

FDA defines emergency use as the use of a test article in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval [21 CFR

56.102(d)]. If all conditions described in 21 CFR 56.102(d) exist, then the emergency exemption from prospective IRB approval found at 21 CFR 56.104(c) may be used.

Life-threatening, for the purposes of 21 CFR 56.102(d), includes both life-threatening and severely debilitating.

Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life- threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Unless the provisions for an emergency exception from the informed consent requirement are satisfied (see Section G in this section), informed consent must be obtained in accordance with 21 CFR 50 and documented in writing in accordance with 21 CFR 50.27.

The IRB must be notified within 5 working days after an emergency exemption is used (Describe the process for such notifications at the organization (e.g., via the submission of an "Emergency Use Report - Drugs"). The IRB Chair, Vice Chair or designated IRB member will review the report to verify that circumstances of the emergency use conformed to FDA regulations. This must not be construed as IRB approval, as an exemption from the requirement for prospective IRB approval has been invoked. When appropriate, in the event a manufacturer requires documentation from the IRB prior to the emergency use, the IRB Chair or designee will review the proposed use, and, if appropriate, provide a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Investigators are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved drugs.

16.10.1.3 Emergency Exception from the Informed Consent Requirement

An exception under FDA regulations at 21 CFR 50.23(a-c) permits the emergency use of an investigational drug without informed consent when the investigator and an independent physician who is not otherwise participating in the clinical investigation (the emergency use) certify in writing all four of the following conditions:

1. The subject is confronted by a life-threatening situation necessitating the use of the test article;

2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;

3. Time is not sufficient to obtain consent from the subject's LAR; and

4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the subject.

If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent physician determination in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The IRB must be notified within 5 working days when an emergency consent exception is invoked (Describe the process for such notifications at the organization (e.g., via the submission of an "Emergency Use Report" and documentation of the independent physician evaluation)). The IRB Chair, Vice Chair or designated IRB member will review the report to verify that circumstances of the emergency exception conformed to FDA regulations.

16.10.2 Expanded Access to Investigational and Unapproved Medical Devices

As with investigational drugs, unapproved medical devices may normally only be used in humans in an approved clinical trial under the supervision of a participating clinical investigator. However, there are circumstances under which a health care provider may use an unapproved device outside of a clinical study when it is not possible to enroll a patient in a clinical study and the patient is facing life-threatening circumstances or suffering from a serious disease or condition for which no other alternative therapy or diagnostic exists or is a satisfactory option for the patient.

FDA has made the following mechanisms available for these circumstances:

- Emergency Use
- Compassionate Use (or Single Patient/Small Group Access)
- Treatment Use

Investigators seeking access to investigational or unapproved devices under one of the above provisions should work closely with the sponsor or manufacturer, the FDA, and the Baptist HRPP, to ensure that proper regulatory procedures are followed. FDA has made information about expanded access to medical devices available on a website.

16.10.2.1 Compassionate Use of Investigational/Unapproved Medical Devices

The compassionate use provision under expanded access provides a mechanism for

accessing investigational devices for an individual patient or small groups of patients when the treating physician believes the device may provide a diagnostic or treatment benefit. Compassionate use can be used for devices being studied in a clinical trial under an IDE for patients who do not qualify for inclusion in the trial, and for devices for which an IDE does not exist. The following criteria must be satisfied:

1. The patient has a life-threatening or serious disease or condition; and
2. No generally acceptable alternative treatment for the condition exists.

The medical device company must agree to make the medical device available for the proposed compassionate use. FDA and IRB approval are required before the device may be used under the compassionate use provision.

FDA Approval:

When there is an IDE for the device, the IDE sponsor submits an IDE supplement requesting approval for the compassionate use under 21 CFR 812.35(a).

When there is not an IDE for the device, the physician or manufacturer submits the following information to the FDA:

1. A description of the device (provided by the manufacturer);
2. Authorization from the device manufacturer for the use;
3. A description of the patient's condition and the circumstances necessitating treatment or diagnostics (when seeking small group access, the number of patients to be treated;
4. A discussion of why alternative therapies/diagnostics are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition; and
5. The patient protection measures that will be followed, including:
    a. A draft of the informed consent document that will be used;
    b. Clearance from the institution as specified by their policies (see below);
    c. Concurrence (approval) of the IRB Chair or Chair-designated IRB member (prior to FDA request when possible); and
    d. An independent assessment from an uninvolved physician.

When IRB Chair approval cannot be obtained in advance of the submission to the FDA, the request should indicate that approval from the IRB Chair will be obtained prior to use of the device. Proof of IRB Chair approval must be submitted with the follow-up report to the FDA after the patient is treated (or the diagnostic is used).

When the compassionate use is conducted under an IDE, a licensed provider who

receives an investigational device is an "investigator" under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

When the provider obtains an IDE for compassionate use, the provider is considered sponsor-investigator" and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 812, as applicable, including medical device reports and progress reports.

IRB Review

Unless the conditions that permit an emergency use exemption are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational device. When the request is for single-patient compassionate use, the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using medical devices under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the device and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the device.

To request IRB approval for compassionate use, investigators should contact the IRB office and submit the following:

1. A completed Expanded Access Application Form and any additional documentation noted within it;
2. A copy of the information submitted to the FDA (and FDA approval, if available);
3. A copy of the device brochure, Instructions for Use, or other similar documentation that provides information regarding the potential risks and benefits of the device;
4. (Include this if not addressed in an application form) A copy of the plan for treating and monitoring the patient; and
5. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but may condition approval upon receipt of FDA approval. The IRB will provide the investigator with written documentation of its review.

Baptist will consider reliance upon an external IRB for Compassionate Use protocols on a case-by-case basis when the IDE is held by a commercial sponsor and an external IRB has already approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the HRPP/IRB office, to discuss IRB reliance for Compassionate Use protocols.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout the policies apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. Additionally, a follow-up report to the FDA is required following a compassionate use by whomever submitted the original request to the FDA. The report should include summary information regarding patient outcome and any problems that occurred as a result of the device. A copy of the follow- up report to the FDA and any other post-approval submissions or reports to the FDA must be submitted to the IRB within 7 business days of the date of submission to the FDA.

16.10.2.2 Treatment Use of Investigational/Unapproved Medical Devices

During the course of a clinical trial under an IDE, if the data suggest that the device under study is effective, the trial may be expanded to include additional patients with life-threatening or serious diseases under the Treatment Use provision for expanded access. "Treatment Use" also applies to the use of a device for diagnostic purposes under these same conditions. [21 CFR 812.36]

The following criteria must be satisfied for Treatment Use to apply:

1. The device is intended to treat or diagnose a serious or immediately life- threatening disease or condition;

2. There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;

3. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and

4. The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

The IDE sponsor is responsible for applying for a Treatment Use IDE.

A licensed provider who receives an investigational device for treatment use under a Treatment Use IDE is an "investigator" under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

IRB Review

IRB approval is required before the investigational device/diagnostic is used. (Describe

procedures for IRB application here (e.g., following the standard procedures for IRB submissions or by submitting an Expanded Access Application and all associated documentation (see sample in compassionate use section). Describe any additional organizational approval or review requirements.)

Baptist will consider reliance upon an external IRB for Treatment Use IDE protocols on a case-by-case basis when an external IRB has already approved the protocol and is willing to accept review and oversight of additional investigators/sites. Investigators should contact the HRPP/IRB office, to discuss IRB reliance for Treatment Use IDEs.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), for reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. **Additionally**, the semi-annual (applicable until the marketing application is filed) or annual (applicable after the marketing application is filed) progress report from the sponsor must be submitted to the IRB within 7 business days of receipt.

16.10.2.3 Emergency Use of Investigational Devices

FDA regulations permit the emergency use of an investigational or unapproved device without prior approval by the FDA or IRB when an appropriately trained and licensed health care provider determines that:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

FDA expects the provider to make the determination that the above criteria are satisfied, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. Because prior FDA approval is not required, FDA expects providers planning the emergency use of an investigational device to obtain as many of the following as possible:

- An independent assessment from an uninvolved physician;
- Authorization from the device manufacturer;

- Concurrence of the IRB Chair or designee;
- Institutional clearance; and
- Informed consent from the patient or legally authorized representative.

At Baptist, providers planning the emergency use of an investigational or unapproved device must contact the HRPP/IRB office as early in the process as possible and submit the Emergency Use Report – Devices and the supporting documentation called for in the form for review by the IRB Chair or designee. The IRB Chair or designee will review the information provided and determine whether the use conforms with FDA's requirements and expectations and whether the provisions for the protection of the patient appear adequate using the applicable criteria at 21 CFR 50 and 56 as guidelines (e.g., minimization of risks, risk/benefit, safety monitoring, informed consent, etc.).

The emergency use must be reported to the FDA by the IDE Sponsor, when one exists, or by the provider if no IDE exists. Information regarding what to include in the report and where to submit it is available on FDA's website. When the provider is responsible for the FDA report, a copy of the report and any related correspondence must be submitted to the IRB office.

Providers are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved devices.

16.11 Charging Subjects for Investigational Products

FDA regulations do not prohibit charging subjects or their insurers for investigational products so long as those charges comply with specified criteria. FDA approval of such charges does not obviate the investigator's and IRB's responsibility to minimize risks to subjects (Beneficence), to ensure that the risks and burdens associated with research are equitably distributed (Justice), and to ensure that subjects are properly informed and not unduly influenced to accept an otherwise unacceptable risk or cost in order to access a benefit (Respect for Persons). Any costs to subjects or insurers must be described in the IRB application and informed consent document.

16.11.1 Charging for Investigational Medical Devices and Radiological Health Products

IDE regulations allow sponsors to charge for an investigational device; however, the charge may not exceed the amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device [21 CFR 812.7(b)]. Sponsors must justify the proposed charges for the device in the IDE application, state the amount to be charged, and explain why the charge does not constitute commercialization [21 CFR 812.20(b)(8)].

16.11.2 Charging for Investigational Drugs and Biologics

In 2009, FDA updated its rules at 21 CFR 312 regarding charging for Investigational Drugs Under an IDE. These rules:

- Provide general criteria for authorizing charging for an investigational drug [21 CFR 312.8(a)]
- Provide criteria for charging for an investigational drug in a clinical trial [21 CFR 312.8(b)]
- Set forth criteria for charging for an investigational drug for an expanded access for treatment use [21 CFR 312.8(c)]
- Establish criteria for determining what costs can be recovered when charging for an investigational drug [21 CFR 312.8(d)]

Additional information is available in FDA guidance: Charging for Investigational Drugs Under an IND — Questions and Answers.

17 Unanticipated Problems Involving Risks to Subjects or Others

Regulations require an organization to have written procedures for ensuring prompt reporting of "unanticipated problems involving risk to subjects or others" (also referred to as UPs, UAPs, and UPIRTSOs).

This section provides definitions and procedures for the reporting of UAPs to the Baptist IRB. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.2.2.

In conducting its review of protocol deviations, noncompliance, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to an UAP.

17.1 Definitions:

Unanticipated problems involving risk to participants or others. Unanticipated problems involving risks to subjects or others (UAPs) refer to any incident, experience, outcome, or new information that (OHRP):

1. Is unexpected; **and**
2. Is at least possibly related to participation in the research; **and**
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, legal or social harm) than was previously known or recognized

The FDA characterizes UPIRSOs as:

1. unexpected
2. serious, and
3. having implications for the conduct of the study (e.g., requiring a significant, and usually safety-related change in the protocol such as revising inclusion/exclusion criteria to including a new monitoring requirement, informed consent, or investigator's brochure).

UAPs also encompass Unanticipated Adverse Device Effects, as defined below, information that sponsors are required to report to the FDA in IND Safety Reports under 21 CFR 312.32 and Serious Adverse Events (SAEs) that occur in Bioavailability (BA) and Bioequivalence (BE) studies.

Unexpected. The incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the study-related documents, such as the IRB-approved research protocol/research plan and informed consent documents; and the characteristics of the subject population being studied.

Related. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Adverse Event. For the purposes of these policies and procedures, an adverse event (AE) is any untoward or unfavorable occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research. Adverse events encompass both physical and psychological harms. They occur most commonly in the context of biomedical research, although on occasion, they can occur in the context of social and behavioral research.

Serious Unexpected Suspected Adverse Reaction (SUSAR). For research subject to FDA's IND regulations, a Serious Unexpected Suspected Adverse Reaction refers to any suspected adverse reaction to study treatment, including active comparators, that is both serious and unexpected. Sponsors, or sponsor-investigators, are responsible for determining whether an event meets all three components of this definition (i.e., serious & unexpected & suspected adverse reaction), and thus must be reported to the FDA in an IND Safety Report. Investigators are encouraged to consult FDA draft guidance (2021) and final guidance (2012) for information regarding FDA's terminology and its application to safety reporting requirements.

Unanticipated Adverse Device Effect. An Unanticipated Adverse Device Effect (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety, or welfare of subjects [21 CFR 812.3(s)].

17.2 Procedures

17.2.1 Reporting

Adverse events in FDA-regulated clinical trials must be reported to the sponsor in compliance with FDA regulations and sponsor requirements. Unless specifically required by the IRB for a given protocol, the Baptist IRB does not accept reports of adverse events that are not also an unanticipated problem involving risks to subjects or others (UAP).

Investigators must report the following events or issues to the IRB as soon as possible but within **7 working days** after the investigator first learns of the event using the "Interim Event Report" form IRB Manager.

If investigators are uncertain but believe that the event might represent a UAP, a report should be submitted.

Examples of UAPs include:

1. A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome);
2. A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but

uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy);

3. Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveals higher rate in the drug treatment arm versus a control). A summary and analyses supporting the determination should accompany the report;
4. An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator's brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an unanticipated problem involving risk to human subjects. A discussion of the divergence from the expected specificity or severity should accompany the report;
5. A serious AE (SAE) that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). A discussion of the divergence from the expected rate should accompany the report;
6. AEs involving direct harm to subjects enrolled by the local investigator which in the opinion of the investigator or sponsor, may represent an UAP;
7. IND Safety Reports from sponsors that meet the criteria for reporting to the FDA under 21 CFR 312.32. Such reports must be accompanied by confirmation that the sponsor has submitted the report to the FDA. For more information on IND safety reporting, see FDA's guidance "Safety Reporting Requirements for INDs and BA/BE Studies";
8. Any SAE that occurs in a Bioavailability (BA) or Bioequivalence (BE) study
9. Unanticipated Adverse Device Effects (UADEs);
10. Any other AE or safety finding (e.g., based on animal or epidemiologic data) that indicates subjects or others might be at risk of serious, unanticipated harms that are reasonably related to the research. In general, these would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. An explanation of the conclusion should accompany the report.
11. Reports (including reports from DSMBs/DMCs) that indicate that risks are greater than previously known or that indicate that the research should be modified, suspended, or halted.
12. Sponsor or lead investigator/coordinating center-imposed suspension or termination of some or all research activities;

13. An unanticipated event related to the research that exposes subjects or others to potential risk but that does not involve direct harm;
14. A breach of confidentiality or loss of research data (e.g., a laptop or thumb drive is lost or stolen);
15. An unanticipated event related to the research that results in actual harm or exposes individuals other than the research subjects (e.g., investigators, research assistants, students, the public, etc.) to potential risk;
16. New information that indicates increased risk, new risk(s), or decrease to potential benefit from what was previously understood. Examples include:
    a. An interim analysis or safety monitoring report indicates that the frequency or magnitude of harms or benefits may be different than initially presented to the IRB;
    b. A report or publication that indicates the risks, benefits, or merit of the research are different from what was previously understood.

17.2.2 Report Evaluation and Processing

The following procedures describe how UAPs are handled in research at Baptist. Unless specifically required by the IRB, the Baptist IRB does not accept reports of adverse events that do not meet the definition of an UAP.

1. Upon receipt of the Interim Event Report from an investigator, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information.
2. If the IRB Coordinator believes that immediate intervention may be required to protect participants or others from serious harm, reports will be forwarded to the Assistant Director or designee and the IRB Chair or Vice Chair.
3. Upon receipt of a report or complaint from someone other than the investigator or study staff on behalf of the investigator, the IRB Coordinator will notify the investigator when appropriate.
4. The IRB Chair or designated reviewer receives and reviews the report and makes an initial determination as to whether the event represents an UAP. If needed, the Chair or designee may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees).
5. If the reviewer determines that the event may be an UAP, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is a UAP and whether any additional actions, such as those outlined below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator, sponsor, or others (including study committees, such as data monitoring committees, data safety monitoring boards, or steering committees). The results of the review will be recorded in the IRB minutes and communicated to the investigator.

6. Based upon the circumstances, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:

    1. Require modifications to the protocol, plan, or procedures for implantation of the research (Research Plan) as described in the application and other materials submitted to the IRB;
    2. Revise the continuing review timetable;
    3. Modify the consent process;
    4. Modify the consent document;
    5. Provide additional information to current participants (e.g., whenever the information may relate to the subject's rights, welfare, or willingness to continue participation);
    6. Provide additional information to past participants;
    7. Require additional training of the investigator and/or study staff;
    8. Require that current subjects re-consent to participation;
    9. Monitor the research;
    10. Monitor the consent process;
    11. Report or make a referral to appropriate parties within Baptist (e.g., the IO, Corporate Compliance, Risk Management, Privacy);
    12. Suspend IRB approval;
    13. Terminate IRB approval;
    14. Other actions as appropriate given the specific circumstances.

When the IRB determines that an event is an UAP, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 21. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.

18 Non-Compliance

As part of its commitment to protecting the rights and welfare of human subjects in research, Baptist reviews all reports and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research. Additionally, in conducting its review of protocol deviations, unanticipated problems, subject complaints, and other reportable events, the IRB will also consider whether the event or issue was caused by, contributed to, or otherwise related to non- compliance.

All Investigators and other study personnel involved in human subject research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the Institutional Review Board (IRB).

18.1 Definitions:

Allegation of Non-Compliance: Allegation of Non-Compliance is defined as an unproved assertion of non-compliance.

Apparent Noncompliance: an event that appears to constitute noncompliance, but the IRB has not yet made a formal assessment of the event.

Continuing Non-Compliance: Continuing non-compliance is defined as a pattern of non-compliance that, in the judgment of the convened IRB, suggests a likelihood that instances of non-compliance will continue unless the IRB or organization intervenes.

Finding of Non-Compliance: Finding of Non-Compliance is defined as an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, a finding on an audit of an unsigned consent document, or an admission of an investigator of that the protocol/research plan was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and

would therefore represent findings of non-compliance.) Once a finding of non-compliance is proven, it must be categorized as minor non-compliance, serious, sporadic or continuing.

Non-Compliance: Non-compliance is defined as failure to adhere to federal, state, or local regulations governing human subject research, organizational policies related to human subject research, or the requirements or determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious Non-Compliance: Serious non-compliance is defined as non-compliance that, in the judgment of the convened IRB, creates an increase in risks to subjects, adversely affects the rights, welfare or safety of subjects, or adversely affects the scientific integrity of the study. Willful violation of regulations and/or policies may also constitute serious non-compliance.

18.2 Reporting

Investigators and their study staff are required to report instances of possible non-compliance to the IRB within **7 business days** of discovery of this non-compliance. The report must include a complete description of the non-compliance including any personnel involved.

Additionally, any individual or employee may report observed or apparent instances of non-compliance to the Baptist IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or organizational review of these reports.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report a non-compliance, he or she may contact the Assistant Director or IRB Chair or Vice Chair directly to discuss the situation informally.

Corporate Compliance and any other corporate departments will be notified as appropriate.

Complainants may choose to remain anonymous.

18.3 Review of Allegations of Non-Compliance

1. All allegations of non-compliance will be pre-reviewed by the HRPP Director or designee, and if needed, additional information or corrections will be requested, before forwarding the allegation for review by the IRB chair or designated reviewer. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct has occurred, the HRPP Director, IRB Chair or Vice Chair, and when appropriate, the IO will be immediately notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.

2. The IRB Chair or designee receives and reviews the report and makes an initial determination as to whether the event represents non-compliance, and, if so, if the non-compliance may be serious or continuing. If needed, the reviewer may request additional information from the investigator or others. When circumstances warrant, the HRPP Director may bypass this step and assign the report for convened board review.

3. If the reviewer determines that the event or issue is not non-compliance, or is non-compliance but not serious or continuing, they will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions are required. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be documented and communicated to the investigator.

4. If the reviewer determines that the event or issue may be serious or continuing non-compliance, the report will be referred for review by the convened IRB. The convened IRB will determine whether the event is serious or continuing non-compliance. The IRB

will review any proposed corrective and preventative action plans and determine if the plan is acceptable as proposed or if modifications to the plan or additional actions, such as those outline below, are necessary to ensure the protection of human subjects. If needed, the IRB may request additional information from the investigator or others. The results of the review will be recorded in the IRB minutes and communicated to the investigator.

5. When the IRB determines that an event is serious or continuing non-compliance, the IRB may take any of the following actions, or others, to ensure the protection of human subjects:

   a. Requiring modifications to the protocol or research plan

   b. Revising the continuing review timetable

   c. Modifying the consent process

   d. Modifying the consent document

   e. Providing additional information to current participants (e.g., whenever the information may relate to the subject's willingness to continue participation)

   f. Providing additional information to past participants

   g. Requiring additional training of the investigator and/or study staff

   h. Requiring that current subjects re-consent to participation

   i. Monitoring the research

   j. Monitoring consent

   k. Reporting or referral to appropriate parties (e.g., the IO, Compliance, Risk Management, Privacy)

   l. Suspending IRB approval

   m. Terminating IRB approval

   n. Other actions as appropriate given the specific circumstances

6. When the IRB determines that an event is serious or continuing non- compliance, the IRB staff will follow the procedures for reporting to regulatory agencies, sponsors, and organizational officials in Section 21. When appropriate, a preliminary report may be submitted while more information is obtained to inform the determination or actions.

7. Investigators may request that the IRB reconsider its determination by following the procedures in Section 10.4.

18.4 Apparent IRB Non-Compliance

When there has been apparent serious or continuing noncompliance on the part of the IRB (e.g., repeated failure to make a required determination), the Assistant Director will gather the relevant facts and report the matter, with any recommendations, to the IO. The IO may take actions as needed to further investigate the matter (e.g., a directed audit) prior to determining whether the apparent noncompliance is serious or continuing. The IO may also require corrective and preventive actions as warranted to remedy the matter and prevent recurrence. Serious or continuing noncompliance on the part of the IRB will be reported as necessary following the procedures outlined in Section 21.

19 Complaints

Baptist is committed to the ethical conduct of research and the protection of human subjects and addressing promptly any concerns.

The HRPP & IRB will be responsive and sensitive to the complaints or concerns expressed by subjects or others and will respond to all complaints or concerns in a confidential and timely manner.

The PI and all other research team members are responsible for the safety and welfare of all subjects enrolled in their studies. When investigators or team members hear complaints or concerns from subjects, he or she will try to resolve them.

19.1 Reporting Complaints

Investigators conducting research under the auspices of Baptist must report complaints to the Baptist HRPP Office, using the Interim Event Report Form, regardless of the IRB of record. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in the HRPP Policies.

Investigators are encouraged to contact the HRPP Director when they are having difficulty resolving a complaint or concern, and whenever circumstances warrant (e.g., immediate attention is needed).

All complaints, written or oral (including telephone complaints), and regardless of point of origin, are recorded in writing. Within 3 business days of receipt of the complaint, the Assistant Director or designee will generate a letter to acknowledge that the complaint has been received, is being reviewed, and all necessary measures will be taken to address the issue. Complainants may choose to remain anonymous. Baptist maintains a policy of non-retaliation for complaints made in good faith.

The Director of the Human Research Protection Program (HRPP) or designee will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the Baptist Institutional Review Board (IRB) Office. This includes complaints, concerns, and appeals from investigators, research participants and others. When deemed necessary, the IRB Chair and/or the convened IRB will be involved in assessments of complaints.

Upon receipt of the complaint, the HRPP Director will make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If the HRPP Director believes that a suspension may be warranted, the IRB Chair or designee will be notified and the procedures in Section 12 will be followed.

If the complaint may meet the definition of non-compliance, it will be considered an allegation of non-compliance according to Section 18. Corporate Compliance with be notified as applicable.

If the complaint meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Section 17.

If the complaint is actually a query from a subject regarding study procedures, payments not received, etc., it will be forwarded to the investigator/study team for handling. The investigator/study team will be required to document any relevant communications and inform the Baptist or applicable IRB when the matter is closed; If the subject is not satisfied with the outcome, the HRPP Director will review and intervene as appropriate.

20 Other Reportable Information

When research is under the oversight of the Baptist IRB, in addition to UAPs, noncompliance, and complaints, any change to the research implemented without IRB approval and any information that may impact the rights, safety, or welfare of subjects or inform the IRB's oversight of the research must be reported to the IRB within **7 working days** of discovery using the Interim Event Report, as applicable. Investigators conducting research under the oversight of an external IRB must comply with the reporting requirements of the external IRB and the internal reporting requirements outlined in Section 6.2.

Other reportable information includes, but is not limited to, the following:

1. Changes made to the research without prior IRB approval to eliminate apparent immediate hazards to the subject(s);
    a. For device studies subject to FDA's IDE regulations, any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency must be reported to the sponsor and the IRB of record **no later than 5 working days** after the emergency occurred.
2. Protocol Deviations - any variation from the IRB approved research plan that happens without prior review and approval of the IRB and is not necessary to eliminate apparent immediate hazards to the subject(s);
3. Monitoring, audit, and inspection reports in accordance with Section 2.1 of this manual;
4. Notice of:
    a. Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as "OAI" is typically made after FDA has had the opportunity to review the responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and any corresponding compliance actions taken under non-US authorities related to human research protections.
    b. Any litigation, arbitration, or settlements initiated related to human research protections.
    c. Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding human subjects research conducted at or by Baptist or Baptist's program for the protection of human research participants.

    NOTE: The above events (4.a, b, and/or c) must be reported to the HRPP/IRB office via an Interim Event Report **as soon as anyone becomes aware**, with the formal submission within the 7-day timeline as noted above.
5. Sponsor or coordinating center reports;
6. Data Safety Monitoring reports, including reports from DSMBs, DMCs, and others;

7. Enrollment or inclusion of vulnerable populations not previously approved by the IRB for the study (e.g., prisoner, pregnant woman, neonate, child, adult with impaired decision-making capacity);
8. When an existing subject becomes a member of a vulnerable population not previously approved by the IRB for inclusion in the study (e.g., incarceration, pregnancy, or change in decision-making capacity of an already enrolled subject);
9. Holds, suspensions, or terminations of a study, in part or in full, by an investigator, sponsor, or others;
10. Changes that impact the ability of the PI to conduct or supervise the study, temporarily or permanently;
11. Changes that impact the qualifications of investigators or research staff members such as actions taken by regulatory authorities, licensing boards, or credentialing committees;
12. New information that may impact the rights, welfare, or willingness of subjects to continue in the research.

Review Procedures

1. Upon receipt of the report, the IRB staff pre-reviews the submission and, if needed, contacts the investigator for corrections or additional information. If the information provided suggests that subjects may be at risk of harm without immediate intervention or that research misconduct may have occurred, the HRPP Director, IRB Chair, and, when appropriate, the IO will be notified so that they can take any necessary steps to ensure the safety of subjects or investigate the matter.
2. The IRB Chair or designated reviewer receives and reviews the report and if the report may represent a UAP or noncompliance, reviews the report as described in Section 17 or 18. When circumstances warrant, the HRPP Director or IRB Manager may bypass this step and assign the report for convened board review.
3. If the reviewer determines that the event or issue is not noncompliance or an UAP, they will review the event or issue, any proposed corrective and preventative action plans, and determine if any additional actions are needed to ensure the protection of human subjects. As warranted, the reviewer may refer the matter to the convened IRB for review. The results of the review will be recorded in IRB Manager and communicated to the investigator.

21 Reporting to Federal Agencies, Departments and Organization Officials

Federal regulations require prompt reporting to appropriate organization officials and, as applicable, the federal department or agency head or the FDA, of (i) any unanticipated problems involving risks to subjects or others; (ii) any serious or continuing non-compliance with this policy or the requirements or determinations of the Institutional Review Board (IRB); and (iii) any suspension or termination of IRB approval.

When research is under the oversight of an external IRB, the terms of the agreement with that IRB will guide reporting.

21.1 Procedures:

The Assistant Director of the Human Research Protection Program (HRPP) or designee will initiate these procedures as soon as the IRB takes any of the following actions:

1. Determines that an event may be considered an unanticipated problem involving risks to participants or others;
2. Determines that non-compliance was serious or continuing;
3. Suspends or terminates approval of research

The Assistant Director or designee is responsible for preparing reports or letters in accordance with the instructions of the Federal department or agency.

The Assistant Director or designee sends a report to:

1. The IRB Chair
2. Ther IO
3. Applicable Federal departments or agencies
    a. OHRP, if the research is conducted or supported by DHHS, or if an engaged institution's FWA has been voluntarily extended to all non-exempt human subjects research
    b. If the research is conducted or supported by a Common Rule Dept. or Agency other than DHHS, the report is sent to the party identified by the Dept. or Agency. A list of contacts is available on OHRP's Reporting Incidents webpage.
    c. If the study is conducted or supported by a federal dept. or agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the dept. or agency.
    d. FDA, if the study is subject to FDA regulations.

The report will include the following information:

1. The nature of the event (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of IRB approval of research);
2. Name of the institution conducting the research;
3. Title of the research project and/or grant proposal in which the problem occurred;
4. Name of the investigator on the project;
5. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
6. A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision;
7. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol/research plan, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.);
8. Plans, if any, to send a follow-up or final report by the earlier of
    a. a specific date, or
    b. when an investigation has been completed or a corrective action plan has been implemented;
9. Investigator;
10. Sponsor, if the study is sponsored;
11. Supervisor of the investigator;
12. The Privacy Officer of a covered entity, if the event involved unauthorized use, loss, or disclosure of individually identifiable patient information from a covered entity;
13. The Chief Information Security Officer of an organization, if the event involved violations of information security requirements of that organization;
14. Corporate Compliance;
15. Corporate Legal;
16. Chief Executive Officer of the facility where the research was being conducted;
17. Office of Risk Management, if appropriate;
18. Others as deemed appropriate by the IO.

The IRB Chair or designee and the Institutional Official (IO) review the letter and recommend modifications as needed.

The IO is the signatory for all correspondence from the facility.

The Assistant Director ensures that all steps of this policy are completed within 30 working days of the determination. For more serious actions, reporting will be expedited.

22 Investigator Responsibilities

This guidance document describes Baptist Principal Investigator (PI) responsibilities related to the conduct of human subject research.

22.1 Definitions

Within the regulations, the term "investigator" refers to individuals involved in the design, conduct, or reporting of the research. Such involvement could include one or more of the following:

- Designing the research
- Obtaining information about living individuals by intervening or interacting with them for research purposes
- Obtaining identifiable private information about living individuals for research purposes
- Obtaining the voluntary informed consent of individuals to be subjects in research
- Studying, interpreting, or analyzing identifiable private information or data for research purposes.

Principal Investigators (PI)

1. Principal Investigators (PIs) are ultimately responsible for the conduct of research. PIs may delegate tasks to appropriately trained and qualified members of their research team. However, PIs must maintain oversight and retain ultimate responsibility for the proper conduct of the research by those to whom they delegate responsibilities.

2. Baptist staff members and affiliated providers may serve as the PI or as the sub-investigators on a research project involving human subjects.

3. Any investigator whose status is considered to be "in training" (e.g., students) may not serve as a PI but may serve as a co-investigator or sub- investigator. PIs will ensure that research designed and conducted by trainees has sound research design and is appropriately supervised.
4. The Institutional Review Board (IRB) recognizes one PI for each study. The PI has ultimate responsibility for the research activities. The exception to this is federally funded research with federally approved Multiple PI plans which specifically delineate the responsibilities of the PIs at each site.

5. Studies that require expertise or skills beyond those held by the PI must either be modified or have expertise and skills supplemented by the inclusion of one or more additional qualified co/sub-investigators.

Sub-Investigators

1. A sub-investigator is any individual other than the PI who is involved in the conduct of a research study. Such involvement could include:

    a. Obtaining information about living individuals by intervening or interacting with them for research purposes;

b. Obtaining identifiable private information about living individuals for research purposes;

c. Recruiting and obtaining the voluntary informed consent of individuals to be subjects in research; and

d. Studying, interpreting, or analyzing identifiable private information or data for research purposes.

22.2 Responsibilities

In order to satisfy the requirements of this policy, investigators who conduct research involving human subjects must fulfill, but not be limited to, the following requirements:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report;
2. Develop a research plan that is scientifically sound and minimizes risk to the subjects;
3. Incorporate into the research plan a plan to ensure the just, fair, and equitable recruitment and selection of subjects;
4. When some or all of the subjects are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons), include additional safeguards in the study to protect the rights and welfare of these subjects;
5. Ensure that the research plan includes adequate provisions for the monitoring of subjects and data to ensure the safety of subjects;
6. Ensure that there are adequate provisions to protect the privacy interests of subjects;
7. Ensure that there are adequate provisions to protect data confidentiality and interests of subjects, including an information security plan that considers the collection, storage, maintenance, analysis, and transmission of data and other identifiable information;
8. Have sufficient resources necessary to protect human subjects, including, but not limited to:

    a. Access to a population that would allow recruitment of the required number of subjects.

    b. Sufficient time to conduct and complete the research.

    c. Adequate numbers of qualified staff.

    d. Adequate facilities.

    e. Necessary equipment.

    f. A plan to ensure proper supervision of the research including a plan for periods of absence or decreased availability.

g. Availability of medical, psychological, or other support that subjects might require during or as a consequence of their participation in the research, when appropriate.

h. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of the state in which the study is conducted and the policies of Baptist;

i. Assure that all study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;

j. Assure that all persons assisting with the research are adequately trained and informed about the protocol/research plan and their specific duties and functions;

k. Promptly report any changes in, addition to, or departure of investigators or research staff to the IRB for evaluation and approval prior to implementation of the change;

l. Protect the rights, safety, and welfare of participants;

m. Ensure that when protected health information (PHI) is used, a legally effective HIPAA authorization is obtained for each subject unless the Privacy Board or IRB has approved a waiver of the requirement;

n. Ensure that the language in the consent form is consistent with that in the protocol/research plan, any associated grant or contract, and, when applicable, in the HIPAA authorization;

o. Obtain and document informed consent and ensure that no human subject is involved in the research prior to obtaining consent or consent/permission from their legally authorized representative, unless a waiver of the requirement has been approved by the IRB;

p. Have a procedure to receive questions, complaints, or requests for additional information from subjects and respond appropriately;

q. Ensure that all information provided to the IRB is accurate and complete so that the IRB may fulfill its responsibilities to review the research and make the required determinations;

r. Ensure that all research involving human subjects receives IRB review and approval in writing or a determination of exemption before research begins;

s. Ensure that all research involving human subjects is reviewed by other experts and organizational components and committees as applicable to the research;

t. Comply with all IRB decisions, conditions, and requirements;

u. Ensure that studies receive timely continuing IRB review and approval as applicable;

v. Report unanticipated problems, deviations, complaints, non- compliance,

suspensions, terminations, and any other reportable events to the IRB;

w. Notify the IRB if information becomes available that suggests a change to the potential risks or benefits, merit, or feasibility of the research;Obtain IRB review and approval before changes are made to the research protocol unless a change is necessary eliminate apparent immediate hazards to the subject(s);

x. Seek assistance from the IRB or Assistant Director when in doubt about whether proposed research requires IRB review;

y. Retain records for the time period and in the manner required by applicable regulations, contractual agreements, and organizational policies

z. Additional investigator responsibilities, including specific responsibilities for investigators engaged in FDA-regulated research, are described elsewhere in this document.

22.3 Investigator Responsibilities for Training and Supervision of Participating Staff and Faculty

1. The Principal Investigator has the responsibility to assure that all participating faculty and research staff:

2. Observe applicable laws, regulations, and institutional policies and procedures.

3. Are qualified and appropriately trained for their roles and responsibilities and adhere to the provisions of the IRB-approved protocol.

4. Complete CITI Human Subjects Protection on-line training.

5. Complete Baptist Standards of Conduct and HIPAA research training, as applicable.

6. Complete Financial Conflict of Interest (FCOI) training and complete a financial disclosure form.

22.4 Investigator Records

Investigator research records, including, but not limited to, signed consent forms and HIPAA authorizations, subject records and data, test article records, IRB records (submission materials, IRB determinations and associated documentation, correspondence to and from the IRB, etc.), and sponsor/grant records must be retained in accordance with regulatory, organizational, IRB, sponsor or grantor, and journal or publication standards.

Records must be maintained securely with limited access.

Disposal of investigator records must be done in such a manner that no identifying information can be linked to research data.

When research is sponsored or grant-supported, consult the contract, grant terms, or other relevant agreements prior to destroying or transferring any records.

If there are questions or allegations about the validity of the data or the appropriate conduct of

the research, all records must be retained until such questions or allegations have been completely resolved.

The following summarizes a few of the more common regulatory requirements:

OHRP – research records must be retained for at least 3 years after the completion of the research

HIPAA – Research authorizations, or documentation of waivers or alterations of authorization, must be held for a minimum of 6 years after the authorization or waiver/alterations was last obtained or in effect, whichever is later

FDA – Drugs (& biologics classified as drugs) - For a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified

FDA – Devices (& biologics classified as devices) - For a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol

22.5 Investigator Concerns

Investigators who have concerns or suggestions regarding the conduct of research at Baptist, Baptist's HRPP, or the IRB of record should convey them to the Institutional Official, Corporate Compliance, or via the Compliance Hotline or other responsible parties (e.g., supervisor, Chief Executive Officer), when appropriate.

The Institutional Official will consider the issue, and when deemed necessary, seek additional information and convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted. In addition, the Chair of the IRB or the ED will be available to address investigators' questions, concerns and suggestions.

In addition to these Standard Operating Procedures, which are made available on the Baptist website, investigators are also made aware of the process for expressing their concerns via a statement on determination letters, and a link on the Baptist website for concerns or complaints.

23 Sponsored Research

It is Baptist policy that any research conducted under the auspices of the Organization is conducted in accordance with federal guidelines and ethical and legal standards. The following describe the procedures required to ensure that all research meets this requirement.

23.1 Definitions:

Non-sponsored Research: Research that does not have a sponsor. The research may be supported by internal funds or donated effort.

Sponsor: Sponsor means the company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

Sponsored research: Sponsored research means research funded by external entities (public, industry, or private) through a grant or contract that involves a specified statement of work (e.g., the research proposal), including clinical trials involving investigational drugs, devices or biologics.

23.2 Responsibilities

All research related sponsor grants, contracts, and other written agreements will be reviewed by the Baptist Clinical Research Institute and Corporate Legal, with consultation with the IRB, as necessary:

All sponsored studies shall have a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.

In studies where Sponsors conduct research site monitoring visits or monitoring activities remotely, the sponsor contracts have a written agreement with the Sponsor that the Sponsor promptly reports (no longer than within 30 days) to Baptist findings that could affect the safety of participants or influence the conduct of the study.

When the Sponsor has the responsibility to conduct data and safety monitoring, the sponsor agreement shall include written provisions that address the monitoring of data to ensure the safety of participants and for the purpose of providing data and safety monitoring reports to Baptist.

Sponsor agreements shall include written provisions addressing plans for disseminating findings from the research and shall define the roles that investigators and Sponsors will play in the publication or disclosure of results.

The Sponsor agreement shall include a written provision addressing the Sponsor's duty to notify the investigator or Baptist when participant safety could be directly affected by study results after the study has ended in order for Baptist to consider informing participants. The Sponsor's reporting obligation shall continue for two years following completion of the study conducted under the contract.

Payment in exchange for referrals of prospective participants from investigators (physicians) ("finder's fees") is not permitted. Similarly, payments designed to accelerate recruitment that

are tied to the rate or timing of enrollment ("bonus payments") are also not permitted.

24 Conflict of Interest in Research

It is Baptist policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest in the conduct of research.

Conflicts of interest (COI) in research can be broadly described as any interest that competes with an organization's or individual's obligation to protect the rights and welfare of research subjects, the integrity of a research study, or the credibility of the research program. Conflicts of interest can be financial or non-financial. In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively managed and disclosed when they cannot be eliminated.

Compliance with the Baptist Conflict of Interest and Commitment Policy (S.AD.1006- 05) and federal regulations under 42 CFR Part 50, Subpart F is required. Baptist maintains a Compliance Committee (CC) that addresses potential Conflicts of Interest in research. The Assistant Director collaborates with Corporate Compliance and the CC to ensure that COI of researchers and research staff (researchers) are identified and addressed before the IRB completes its review of any research submission.

24.1 Researcher Conflict of Interest

Identifying potential conflicts of interest for researchers is part of the IRB Office's preliminary review for all submissions.

If a potential conflict for a researcher is identified, the IRB Office notifies the Corporate Compliance Office and requests a review of the researchers' disclosure(s).

The Corporate Compliance Office responds to the IRB Office that either no COI was identified or that one or more researchers has an interest that requires evaluation by the Compliance Committee.

In the event a conflict is identified that requires disclosure or management, the Corporate Compliance Office will provide the IRB with a written summary of the conflict and, if applicable, an approved Conflict of Interest Management and Monitoring Plan (CMP).

If the Compliance Committee has not completed its review when the submission is scheduled to be reviewed by the convened IRB, the IRB will either defer review of the submission or prohibit the conflicted researcher from participating in the research activities until the Compliance Committee review process is completed and the results are made available to the IRB.

When the research is under an external IRB, any conflicts identified and any resulting CMPs created as the result of COI review are provided to the external IRB in accordance with the IRB reliance agreement.

24.1.1 Evaluation of COI

The IRB will review COI and CMP to determine whether:

1. The COI affects the rights or welfare of research subjects,
2. The COI might adversely affect the integrity or credibility of the research or the research program, and
3. The CMP effectively protects research subjects and the integrity and credibility of the research and the research program.

The IRB will consider:

1. How the research is supported or financed;
2. The nature and extent of the conflict;
3. The role and responsibilities of the conflicted individual in the design, conduct, and reporting of the research; and
4. The ability of the conflicted individual to influence the outcome of the research.

24.1.2 Management of COI

The IRB has final authority to determine whether the research, the COI, and the CMP, if any, allow the research to be approved.

The IRB shall either affirm or request changes to strengthen any CMP. The IRB can require additional measures to manage a COI so that the research may be approved. However, the IRB cannot weaken a CMP approved by the Compliance Committee. For example, in addition to the CMP, the IRB may require:

1. Disclosure of the COI to subjects through the consent process;
2. Modification of the research plan or safety monitoring plan;
3. Monitoring of research by a third party;
4. Disqualification of the conflicted party from participation in all or a portion of the research;
5. Appointment of a non-conflicted PI
6. Divestiture of significant financial interests
7. Severance of relationships that create actual or potential conflicts.

In the event the conflict cannot be effectively managed the IRB may disapprove the research.

24.2 IRB Member Conflict of Interest

No IRB member or alternate may participate in the review of any research submission in which the member has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB member to disclose any COI related to a submission for review and recuse him/herself from the deliberations and vote by leaving the room.

All IRB members complete a disclosure annually. This ensures that IRB members are not assigned reviews for which the member has a conflict and appropriate recusal during convened meetings. IRB members or consultants may be considered to have a conflicting interest requiring recusal when they, or an immediate member of their family, have any of the following:

1. Involvement in the design, conduct, and reporting of the research;

2. Significant financial interests (See Baptist Administrate Policy S.AD.1006.05 Conflict of Interest and Commitment for a definition of significant financial interests) related to the research being reviewed;

3. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a study.

The IRB Chair or Vice-Chair asks IRB members at the beginning of each convened meeting if any members have a COI regarding any of the items to be reviewed and reminds members that they must recuse themselves by leaving the room during the discussion and vote of the specific agenda item. If a conflicted member is participating by conference call, videoconference or web meeting, the member's participation (connection) is terminated for discussion and voting.

IRB members with a conflicting interest are excluded from being counted towards quorum. Recusals of members with COIs are recorded in the minutes.

24.3 Institutional Conflict of Interest

An Institutional Conflict of Interest in research (Institutional COI) describes a situation in which the financial interests of an institution or an institutional official, acting within his or her authority on behalf of the institution, may unduly affect or appears to affect the conduct of research or other related activities of the institution.

Institutional COIs are of concern when institutional financial interests create the potential for inappropriate influence over the institution's activities. Baptist outlines the mechanism to deal with organizational conflict in the Institutional Conflict of Interest Policy. This policy is intended to protect against risks to research integrity, research participants and the mission that may result from Institutional COIs in research. The purpose of this policy is to promote the highest ethical standards in the conduct of research in situations where institutional conflicts of interest may occur, and to determine those instances when an Institutional COIs are unacceptable. See also policy S.AD.1053.01 Institutional Financial Conflict of Interest in Research.

24.4 Recruitment Incentives

Payment arrangements among sponsors, organizations, investigators, and those referring research participants present a conflict of interest and may place participants at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective participants (finder's fees) is not permitted. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (bonus payments) is also not permitted.

25 Participant Outreach

Baptist is committed to ensuring that educational opportunities are offered to research participants, prospective research participants, and community members, which will enhance their understanding of research involving human participants at Baptist and provide them the opportunity to provide input and express concerns. The following procedures describe how Baptist fulfils that responsibility.

25.1 Outreach Resources and Educational Materials

The BaptistOnline.org website has separate web pages for Research at Baptist, the Baptist Cancer Center (BCC), and the Baptist Clinical Research Institute (BCRI) that the public can access. Each of these web pages dedicates a section for research participants. These websites include resources, such as Frequently Asked Questions (FAQs); a general overview of clinical trials; and listings of clinical trials available, cancer support groups, public research events, and relevant external research-related links.

The HRPP/IRB, BCRI, and the BCC Research web pages include information regarding how to contact Baptist with any questions or concerns about specific research projects or research in general.

The BCRI, BCC, and HRPP/IRB websites include a "Contact Us" link that allows community members to ask questions, express concerns, or provide feedback.

25.2 Evaluation

On an annual basis, Baptist evaluates its outreach activities and makes changes when appropriate. To formally evaluate its outreach activities, the Assistant Director will review:

1. The specific community outreach activities being used;
2. Whether or not these community outreach activities have an evaluative component (e.g., evaluation instrument distributed to participants); and if so, whether the feedback was positive, negative, or neutral, and if any suggestions were made that could be used to enhance future activities;
3. The number of times the Research Events web page is visited;
4. Feedback provided via the "Contact Us" mechanism on the BCRI, BCC, and HRPP/IRB web pages;
5. Feedback provided from other sources (unaffiliated IRB members, investigators, research staff, students, etc.)

The results of the review will be used to establish both the adequacy of current outreach activities and any additional resources that may be needed to meet the needs of the research community regarding participant outreach.

26 Health Insurance Portability and Accountability Act (HIPAA)

The *Health Insurance Portability and Accountability Act of 1996* (HIPAA) required the creation of a Privacy Rule for identifiable health information. While the primary impact of the Privacy Rule is on the routine provision of and billing for health care, the Rule also affects the conduct and oversight of research.

The Privacy Rule defines individually identifiable health information transmitted or maintained by a covered entity in any form (electronic, written or oral) as "protected health information" (PHI) and establishes the conditions under which investigators may access and use this information in the conduct of research.

Except as otherwise permitted, the Privacy Rule requires that a research subject "authorize" the use or disclosure of his/her PHI to be used in research. This authorization is distinct from the subject's consent to participate in research, which is required if the research is subject to the Common Rule, FDA regulations, and/or state laws that provide additional protection for research involving certain categories of health information (such as information derived from HIV/AIDS testing, genetic testing, and mental health records). When research consent is not required by regulation or law (e.g., for exempt research) or the requirement for research consent has been waived by an IRB, the requirements for authorization still apply unless an IRB or Privacy Board has determined that the criteria for a waiver of the authorization requirement are satisfied.

HIPAA allows both use and disclosure of PHI for research purposes. The HIPAA Privacy Rule establishes the conditions under which PHI may be used or disclosed by Covered Entities for research purposes.

Except as otherwise permitted, the Privacy Rule requires that a research participant "authorize" the use or disclosure of his/her PHI to be used in research. This authorization is distinct from the research participant's informed consent to participate in research, which is required under the Common Rule and FDA regulations.

Under the Privacy Rule, a HIPAA Authorization may be combined with the informed consent document for research. When the informed consent document is combined with a HIPAA Authorization, 45 CFR part 46 (Common Rule) and 21 CFR part 56 (FDA Regulations) require IRB review of the combined document.

At Baptist, for non-exempt projects that have been granted a waiver of informed consent and for exempt research (or other research not subject to IRB oversight), the Baptist IRB is designated to act upon requests for waivers and alterations of the HIPAA Authorization requirement for research purposes.

26.1 Definitions:

Access: Access means the ability or the means necessary to read, write, modify, or communicate data/information or otherwise use any system resource.

Accounting of Disclosures: Information that describes a Covered Entity's disclosures of PHI other than for treatment, payment, and health care operations; that have occurred during the 6 years (or a shorter time period at the request of the individual) prior to the date of the request

for an accounting.

Alteration of HIPAA Authorization: Waiver of one or more of the requirements of the Privacy Rule.

Authorization: An individual's written permission to allow a covered entity to use or disclose specified PHI for a particular purpose. Except as otherwise permitted by the Privacy Rule, a covered entity may not use or disclose PHI for research purposes without a valid Authorization that includes all of the required elements under the Privacy Rule.

Compound Authorization: Where an authorization for the use and disclosure of PHI is combined with any other legal permission.

Conditioned Authorization: Authorization that conditions treatment, payment, enrollment in a health plan, or eligibility for benefits.

Covered Entity: A health plan, a health care clearinghouse, or a health care provider who transmits health information in electronic form in connection with a transaction. For purposes of this policy it would be a Baptist affiliated entity (i.e. hospital, clinic). Data Use Agreement: A contractual document used for the transfer of data, where the data is subject to some restrictions on its use.

De-identified: Data is considered de-identified under HIPAA when they do not identify an individual, and there is no reasonable basis to believe that the data can be used to identify an individual. The Privacy Rule defines two methods for de- identifying PHI:

1. When the PHI is stripped of all 18 HIPAA-defined identifying elements and the covered entity does not have actual knowledge that the information could be used alone or in combination with other information to identify an individual who is a subject of the information (Safe Harbor method); or

2. When an appropriate expert determines that the risk is very small that the information could be used, alone or in combination with other reasonably available information, by an anticipated recipient to identify an individual who is a subject of the information (Expert Determination method).

Designated Record Set: A group of records maintained by or for a Covered Entity that may include:

1. patient medical and billing records
2. enrollment, payment, claims adjudication, and case or medical management record systems maintained by or for a health plan; or
3. used, in whole or in part, to make decisions about individuals.

A record is any item, collection, or grouping of information that includes PHI and is maintained, collected, used, or disseminated by or for a covered entity.

Disclosure: The release, transfer, provision of access to, or divulging of information in any other manner outside the entity holding the information.

Health Information: Health Information means any information, including genetic information, whether oral or recorded in any form or medium, that:

1. Is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and
2. Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

Individually Identifiable Health Information: Information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Limited Data Set: Information from which identifiers have been removed. Specifically, as it relates to the individual or his or her relatives, employers or household members, all the 16 identifiers must be removed in order for health information to be a Limited Data Set. Limited Data Sets may be used or disclosed, for purposes of research, public health, or health care operations, without obtaining either an individual's Authorization or a waiver or an alteration of Authorization for its use and disclosure, only if the covered entity obtains satisfactory assurances in the form of a Data Use Agreement. Limited Data Sets are not de-identified information under the Privacy Rule.

Minimum Necessary: Rule requires a Covered Entity when using, disclosing, or requesting PHI to make reasonable efforts to limit PHI to the minimum amount necessary to accomplish the intended purpose of the use, disclosure or request. Privacy Board: A review body established to act upon requests for a waiver or an alteration of the HIPAA Authorization requirement under the HIPAA Privacy Rule for uses and disclosures of PHI for a particular research study.

Protected Health Information (PHI): PHI is individually identifiable health information transmitted by electronic media, maintained in electronic media, or transmitted or maintained in any other form or medium. PHI excludes individually identifiable health information in education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g, records described at 20 U.S.C. 1232g(a)(4)(B)(iv), employment records held by a Covered Entity in its role as employer and regarding a person who has been deceased for more than 50 years.

Psychotherapy Notes: Psychotherapy notes means notes recorded (in any medium) by a health care provider who is a mental health professional documenting or analyzing the contents of conversation during a private counseling session or a group, joint, or family counseling session and that are separated from the rest of the individual's medical record. Psychotherapy notes excludes medication prescription and monitoring, counseling session start and stop times, the modalities and frequencies of treatment furnished, results of clinical tests, and any summary of the following items: Diagnosis, functional status, the treatment plan, symptoms,

prognosis, and progress to date.

Research: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. This includes the development of research repositories and databases for research.

Unconditioned Authorization: Authorization for another purpose for which treatment, payment, enrollment, or eligibility may not be conditioned.

Use: With respect to individually identifiable health information, the sharing, employment, application, utilization, examination, or analysis of such information within the entity that maintains such information.

Waiver of HIPAA Authorization: The documentation by which the IRB has waived or altered the Privacy Rule's requirement that an individual must authorize a Covered Entity to use or disclose the individuals PHI for research purposes.

Workforce: Employees, volunteers, trainees, and other persons whose conduct, in the performance of work for a Covered Entity, is under the direct control of the Covered Entity, whether or not they are paid by the Covered Entity.

26.2 The IRB's Role under the Privacy Rule

In the course of conducting research, researchers may obtain, create, use, and/or disclose individually identifiable health information. Under HIPAA, researchers within Baptist are permitted to use and disclose protected health information for research with individual authorization, or without individual authorization under limited circumstances (e.g., if the IRB/Privacy Board approves an alteration of authorization, or a partial or full waiver, based on specific criteria). Such limited circumstances would include the review of medical record information for a 'chart review' study (full waiver), review of medical records for recruitment purposes (partial waiver), or for obtaining but not documenting authorization (alteration of authorization).

Under the Privacy Rule, IRBs gained authority to consider, and act upon, requests for a partial or complete waiver or alteration of the Privacy Rule's Authorization requirement for uses and disclosures of PHI for research. Although Department of Health and Human Services (HHS) and FDA Protection of Human Subjects Regulations include protections to help ensure the privacy of research participants and the confidentiality of information, the Privacy Rule supplements these protections by requiring Covered Entities to implement specific measures to safeguard the privacy of PHI. If certain conditions are met, an IRB may grant a waiver or an alteration of the HIPAA Authorization requirement for research uses or disclosures of PHI.

The Baptist IRB, and when mutually agreed, the external IRBs upon which Baptist relies, fulfil the functions of a Privacy Board (required by HIPAA) for human subjects research. When the IRB determines that research participants should sign a HIPAA Authorization in order to use or disclose PHI for research, research participants are to sign the HIPAA Authorization as a part of the informed consent process for participation in the research study.

When acting upon a request to waive or alter the Authorization requirement, an IRB must follow the procedural requirements of the HHS Protection of Human Subjects regulations and, if applicable, FDA regulations, including using either the normal review procedures (review by the convened IRB) or the expedited review procedures.

When a request for a waiver or an alteration of the Authorization requirement is considered by the convened IRB, a majority of the IRB members must be present at the meeting, including at least one member whose primary concerns are in non-scientific areas. In order for an approval of a waiver or an alteration of the Privacy Rule's Authorization requirement to be effective, it must be approved by a majority of the IRB members present at the convened meeting.

Expedited review of a request for a waiver or an alteration of the Authorization requirement is permitted if the research qualifies for expedited review under Common Rule requirements (See Section 11.1). 45 CFR 46.110 and 21 CFR 56.110 permit an IRB to use an expedited review procedure to review minor changes in previously approved research. A modification to a previously approved research protocol, which only involves the addition of an Authorization for the use or disclosure of PHI to the IRB-approved informed consent, may be reviewed by the IRB through an expedited review procedure, because this type of modification may be considered to be no more than a minor change to research. If expedited review procedures are appropriate for acting on the request, the review may be carried out by the IRB Chair or by one or more experienced reviewers designated by the Chair from among the IRB members. A member with a conflicting interest may not participate in an expedited review. If an IRB uses expedited review procedures, it must adopt methods for keeping all its members advised of all requests for waivers or alterations of the Authorization requirement as well as those requests that have been granted under an expedited review procedure.

IRB documentation of approval of a waiver or alteration of the Authorization requirement includes:

1. The identity of the approving IRB
2. The date on which the waiver or alteration was approved
3. A statement that the IRB has determined that all the specified criteria for a waiver or an alteration were met
4. A brief description of the PHI for which use or access has been determined by the IRB to be necessary in connection with the specific research activity
5. A statement that the waiver or alteration was reviewed and approved under either normal or expedited review procedures
6. The required signature of the IRB Chair or the Chair's designee.

Baptist will not release PHI to investigators without individual authorization or proper documentation of an IRB approval of a Waiver or Alteration of the requirement. In order to ensure that appropriate approvals are in place and that uses of patient information for research are in accordance with Baptist standards, Baptist does not accept Waivers or Alterations approved by a non- Baptist Privacy Board or HRPP.

26.3 HIPAA Authorization

The Privacy Rule permits Covered Entities to use or disclose PHI for research purposes when a research participant authorizes the use or disclosure of information about him or herself. To use or disclose PHI with authorization by the research participant, the Covered Entity must obtain an authorization that satisfies the requirements of 45 CFR 164.508(c).

At Baptist, when HIPAA authorization from the subject is required, the required language is to be incorporated into the informed consent document. Template informed consent documents, which include HIPAA Authorization language, are available from the Baptist IRB.

Once executed, a signed copy of the consent form with the approved HIPAA Authorization must be provided to the individual providing the authorization at the time of consent. The original signed consent form(s) must be retained in the research file or regulatory binder, scanned into the research participant's medical record and retained in accordance with applicable federal and state laws and the Baptist retention policy, or six years, whichever is later.

A research participant has the right to revoke his/her HIPAA Authorization at any time. A research participant may not revoke a HIPAA Authorization to the extent the Covered Entity has acted in reliance on the HIPAA Authorization. For research uses and disclosures, this reliance exception at § 164.508(b)(5)(i) permits the continued use and disclosure of PHI already obtained pursuant to a valid HIPAA Authorization to the extent necessary to preserve the integrity of the research study. The reliance exception would not permit a Covered Entity to continue disclosing additional PHI to a researcher or to use for its own research purposes information not already gathered at the time a research participant withdraws his or her HIPAA Authorization.

When an authorization is obtained for research purposes, the Privacy Rule requires that it pertain only to a specific research study, not to non-specific research or to future, unspecified projects. The Privacy Rule considers the creation and maintenance of a research repository or database as one specific research activity, the subsequent use or disclosure by a Covered Entity of information from the database for a specific research study requires separate authorization unless a waiver of the requirement is granted.

When a HIPAA Authorization permits disclosure of PHI to a person or organization that is not a Covered Entity (such as a sponsor or funding source) or subject to HIPAA, HIPAA does not protect the PHI disclosed to such person/entity. However, federal and state laws and other agreements between the Covered Entity and recipient such as a Business Associate Agreement (BAA), Data Use Agreement (DUA), or Confidentiality Agreement may establish continuing protections for the disclosed information. Under the HHS Protection of Human Subjects regulations or the FDA Protection of Human Subjects regulations, an IRB may impose further restrictions on the use or disclosure of research information to protect research participants.

Authorization Core Elements:

1. A description of the PHI to be used or disclosed, identifying the information in a specific and meaningful manner.

2. The names or other specific identification of the person or persons (or class of persons) authorized to make the requested use or disclosure.

3. The names or other specific identification of the person or persons (or class of persons) to whom the Covered Entity may make the requested use or disclosure.

4. A description of each purpose of the requested use or disclosure.

5. An expiration date or expiration event that relates to the research participant or to the purpose of the use or disclosure ("end of the research study" or "none" are permissible for research, including for the creation and maintenance of a research database or repository).
6. Signature of the research participant and date. If the individual's legally authorized representative signs the HIPAA Authorization, a description of the representative's authority to act for the research participant must also be provided.

Authorization Required Statements:

In addition to the core elements, the HIPAA Authorization must contain statements adequate to place the research participant on notice of all the following:

1. A statement of the individual's right to revoke his/her HIPAA Authorization in writing and how to do so, and, if applicable, the exceptions to the right to revoke his/her HIPAA Authorization or reference to the corresponding section of the Covered Entity's notice of privacy practices.

2. The ability or inability to condition treatment, payment, enrollment, or eligibility of benefits on the HIPAA Authorization, including research-related treatment or the consequences to the research participant if refusing to sign the HIPAA Authorization if the Covered Entity can condition treatment, payment, enrollment, or eligibility of benefits on failure to obtain such HIPAA Authorization.

3. A statement of the potential risk that PHI will be re-disclosed by the recipient. This may be a general statement that the Privacy Rule may no longer protect health information disclosed to the recipient.

26.4 Waiver or Alteration of the Authorization Requirement

Under the Privacy Rule, researchers are permitted to use and disclose PHI with HIPAA Authorization from the research participant. In certain circumstances a waiver from this requirement may be obtained from the IRB where it may not be practical to conduct research without the waiver. However, a waiver of HIPAA Authorization does not mean that the research is exempt from HIPAA requirements. It only means that the researcher does not need to obtain signed HIPAA Authorization(s) from the research participant to use and disclose their PHI.

For research uses and disclosures of PHI, an IRB may approve a waiver or an alteration of the authorization requirement in whole or in part. A complete waiver occurs when the IRB determines that no authorization will be required for a Covered Entity to use and disclose PHI for

a particular research project. A partial Waiver of Authorization occurs when the IRB determines that a Covered Entity does not need authorization for all PHI uses and disclosures for research purposes, such as accessing PHI for research recruitment purposes. An IRB may also approve a request that removes some PHI, but not all, or alters the requirements for an authorization (an alteration).

In order for an IRB or Privacy Board to waive or alter authorization, the Privacy Rule (45 CFR 164.512(i)(2)(ii)) requires the IRB or Privacy Board to determine the following:

1. The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
    a. An adequate plan to protect health information identifiers from improper use and disclosure;
    b. An adequate plan to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
    c. Adequate written assurances that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule;
2. The research could not practicably be conducted without the waiver or alteration; and
3. The research could not practicably be conducted without access to and use of the PHI.

The Privacy Rule allows institutions to rely on a waiver or an alteration of Authorization obtained from a single IRB or Privacy Board to be used to obtain or release PHI in connection with a multi-site project.

At Baptist, PHI may not be disclosed for the purposes of research pursuant to a waiver provided by a non-Baptist Privacy Board without the approval of the Assistant Director or IRB.

26.5 Activities Preparatory to Research

Under the preparatory to research provision of the Privacy Rule, a covered entity may permit a researcher to use PHI for purposes preparatory to research such as assessing the feasibility of conducting a research project, developing a grant application or protocol, or identifying potential subjects.

The covered entity must obtain from the investigator representations, either in writing or orally, that (1) the use or disclosure of the PHI is solely to prepare a research protocol or for similar purposes preparatory to research, (2) that the investigator will not remove any PHI from the covered entity (e.g., physically taken out of a facility, or downloaded and retained on the investigator's device) in the course of the review, and (3) the PHI for which access is sought is necessary for the research purpose. [45 CFR 164.512(i)(1)(ii)]

Federal guidance has drawn a distinction between activities that may be undertaken by a researcher who is a member of the covered entity's workforce, e.g., an employee of the covered entity, and a researcher who is not part of the covered entity's workforce. This guidance indicates that researchers may use PHI under the preparatory to research provision to *identify*

potential study participants, so long as no PHI is removed from the covered entity and the remaining two representations set forth above can be made. However, the guidance also indicates that researchers may not use PHI obtained pursuant to the "preparatory to research" provision to *contact* potential study subjects unless (i) the researcher is a member of the covered entity's workforce, or (ii) the researcher enters into a BAA with the covered entity. Therefore, if the researcher is not a workforce member or business associate of the covered entity, then the researcher may contact potential subjects only pursuant to a partial waiver of authorization from the cognizant IRB or privacy board, or pursuant to the Authorization of the subject.

At Baptist, this is accomplished by the researcher submitting a "Research Privacy Application" for Review of Protected Health Information Preparatory to Research" form and approval from the Corporate Privacy and Security Department.

26.6 Research Using Decedent's Information

The HIPAA Privacy Rule protects the individually identifiable health information about a decedent for 50 years following the date of death of the individual. When a researcher seeks to use PHI from decedents for a research protocol, the researcher must (1) obtain authorization from the personal representative of the decedent (i.e., the person under applicable law with authority to act on behalf of the decedent or the decedent's estate), (2) obtain a waiver of the requirement to obtain authorization from an IRB or Privacy Board, or (3) attest to the covered entity holding the PHI that the use or disclosure is solely for research on the PHI of decedents, that the PHI being sought is necessary for the research, and, if requested by the covered entity, provide documentation of the death of the individuals about whom information is being sought.

At Baptist, the attestation option referenced above is accomplished by obtaining approval from the Corporate Privacy & Security Department.

26.7 Future Uses: Databases and Repositories

The Privacy Rule recognizes the creation of a research database or a specimen repository to be a research activity if the data/specimens to be stored contain PHI. When researchers establish a database or repository containing PHI for the purposes of future research or intend to maintain PHI following completion of a primary study for potential future research use, individual authorization for the **storage** of PHI for such future research must be sought unless the IRB has determined that the criteria for a waiver of the authorization requirement are satisfied. See Section 26.4 of this Standard Operating Procedures manual for a discussion of waivers of authorization.

An authorization for use and/or disclosure of the stored PHI for **future research** must describe the future research uses and/or disclosures in sufficient detail to allow the potential subject to make an informed decision. The Rule does not require that an authorization describe each specific future study if the particular studies to be conducted are not yet determined. Instead, the authorization must adequately describe future purposes such that it would be reasonable for the subject to expect that their PHI could be used or disclosed for such research. When developing the description of potential future research uses, the investigator should be cognizant of uses of information/specimens that the community may consider particularly sensitive, such as genetics,

mental health, studies of origin, and use of tissues that may have cultural significance, including whether any state laws may impose additional consent requirements with respect to any of these sensitive categories of information.

The authorization for future research can be a stand-alone document or may be incorporated into the authorization for the establishment of a database or repository or for the primary study unless the research involves the use or disclosure of psychotherapy notes. Authorizations for the use or disclosure of psychotherapy notes can only be combined with another authorization for a use or disclosure of psychotherapy notes.

If the authorization for future research is combined with the authorization for the primary study, the authorization must clearly differentiate between the authorization for the primary study and the authorization for the unspecified future research activities and allow the subject to opt-in to the future research.

It is important to note that securing a HIPAA authorization for unspecified future research activities may not, by itself, satisfy all applicable legal consent requirements. The Common Rule, FDA regulations, and state laws also must be considered, as applicable, in evaluating whether the information (including PHI) or identifiable biospecimens may be used for future research projects.

The HIPAA Authorization for research uses and disclosures of PHI does not have an expiration date, the final Rule at § 164.508(c)(1)(v), requires that this fact be stated on the HIPAA Authorization form. HHS has provided that the statement "none" or similar language be sufficient to meet the requirement for a Covered Entity to use or disclose PHI for the creation or maintenance of a research database or repository.

26.8 Corollary and Sub-studies

Consistent with the discussion above relating to future uses of research databases or repositories, the Privacy Rule mandates that subject participation in corollary or sub-studies not essential to the primary aims of the research, such as when PHI from an interventional clinical trial is used to create or to contribute to a central research repository, must be on a voluntary, "opt-in" basis. This is particularly important when the primary research offers a potential direct benefit to the research subject, such as treatment, that might compel the potential subject to agree to an ancillary study, even if the subject would prefer not to do so.

HIPAA reinforces this ethical principle by explicitly stating that authorization for "unconditioned" activities, for which there is no associated treatment, benefit or other effect on the individual subject associated with participation, cannot be required. The published preamble to HIPAA Omnibus clarifies the basis for this position, and the requirement that authorization for unconditioned activities involve a clear opt-in mechanism, stating:

> "This limitation on certain compound authorizations was intended to help ensure that individuals understand that they may decline the activity described in the unconditioned authorization yet still receive treatment or other benefits

or services by agreeing to the conditioned authorization." and "an opt out option does not provide individuals with a clear ability to authorize the optional research activity, and may be viewed as coercive by individuals."

As with authorization for future research, it is acceptable to combine in a single document the authorization for a conditioned activity, such as a clinical trial, with authorization for an unconditioned activity such as a corollary or sub-study that does not directly benefit or effect the individual participant, provided that:

1. The authorization clearly differentiates between the conditioned and unconditioned research activities;

2. The authorization clearly allows the individual the option to opt in to the unconditioned research activities; and

3. Sufficient information is provided for the individual to be able to make an informed choice about both the conditioned and unconditioned activities.

Separate authorization must be obtained for each research activity that involves the use and disclosure of psychotherapy notes. For example, authorization for the use and disclosure of psychotherapy notes for a clinical trial cannot be combined with an authorization for the use and disclosure of those psychotherapy notes for a corollary research activity.

26.9 De-identification of PHI under the Privacy Rule

Covered Entities may use or disclose health information that is de-identified without restriction under the Privacy Rule. The "Safe Harbor" method permits a Covered Entity to de-identify data by removing all 18 data elements that could be used to identify the individual or the individual's relatives, employers, or household members. The covered entity also must have no actual knowledge that the remaining information could be used alone or in combination with other information to identify individuals. Under this method, the identifiers that must be removed are the following:

1. Names

2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial three digits of a ZIP Code if, according to the current publicly available data from the Bureau of the Census:

    a. The geographic unit formed by combining all ZIP Codes with the same three initial digits contains more than 20,000 people.
    b. The initial three digits of a ZIP Code for all such geographic units containing 20,000 or fewer people are changed to 000.

3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older.
4. Telephone numbers
5. Facsimile numbers
6. Electronic mail addresses
7. Social security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers, including license plate numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLS)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including fingerprints and voiceprints
17. Full-face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code, unless otherwise permitted by the Privacy Rule for re-identification

Alternatively, a qualified statistician may certify that the risk is very small that health information could be used, alone or in combination with other available information, to identify individuals. The qualified statistician must document the methods and results of the analysis that justify such a determination. This analysis must be retained by the covered entity for 6 years from the date of its creation or when it was last acted on, whichever is later.

The Privacy Rule permits a covered entity to assign to, and retain with, the de- identified health information, a code or other means of record re-identification if that code is not derived from or related to the information about the individual and is not otherwise capable of being translated to identify the individual. The covered entity may not use or disclose the code or other means of record identification for any other purpose and may not disclose its method of re- identifying the information.

NOTE: Data that is considered de-identified under HIPAA may still be considered human subject data under the Common Rule, particularly when working with a small data set that can be further divided into smaller subsets. Additionally, while coded information may be de-identified under HIPAA, if the investigator holds or has the ability to access both the code and the

data, the information is considered identifiable private information under the Common Rule.

26.10 Limited Data Sets and Data User Agreements

Limited Data Sets are data sets stripped of certain direct identifiers. Limited Data Sets may be used or disclosed only for public health, research, or health care operations purposes. Because Limited Data Sets may contain identifiable information, they are still PHI and as such are not considered de-identified under the Privacy Rule. Unlike de-identified data, PHI in Limited Data Sets may include: addresses other than street name or street address or post office boxes, all elements of dates (such as admission and discharge dates) and unique codes or identifiers not listed as direct identifiers. The following direct identifiers must be removed for PHI to qualify as a Limited Data Set:

1. Names;
2. postal address information, other than town or city, state, and ZIP code;
3. telephone numbers;
4. fax numbers;
5. email addresses;
6. social security numbers;
7. medical record numbers;
8. health plan beneficiary numbers;
9. account numbers;
10. certificate or license numbers;
11. vehicle identifiers and license plate numbers;
12. device identifiers and serial numbers;
13. URLs;
14. IP addresses;
15. biometric identifiers; and
16. full-face photographs and any comparable images.

Before disclosing a Limited Data Set, a Covered Entity must enter into a Data Use Agreement (DUA) with the recipient, even when the recipient is a member of its workforce. The DUA establishes the parameters around the proposed uses and disclosures of the data, who is permitted to have access to the data, and stipulates that no other use or disclosure will be made other than as permitted by the DUA or as otherwise required by law, no attempt will be made to identify or contact individuals whose data are included in the limited data set, that appropriate safeguards are in place to protect the data from unauthorized use or disclosure, that any agents, including subcontractors, to whom the recipient provides the LDS will agree to the same restrictions and conditions that apply to the recipient, and that the recipient will report any uses or disclosures of the information that they become aware of that are not in keeping with the terms of the DUA.

Data Use Agreements for the purposes of research are available through the Corporate Privacy & Security Department.

26.11 Research Participants' Access to PHI

With few exceptions, the Privacy Rule guarantees individuals access to their medical records and other types of health information. One exception is during a research study, when the research participant's right of access can be suspended while the research is in progress. The research participant must have been notified of and agreed to the temporary denial of access when providing informed consent and HIPAA Authorization. Any such notice must also inform the research participant that the right to access will be restored upon conclusion of the research study. Language accommodating this exclusion is included in the applicable Baptist research informed consent/HIPAA Authorization templates.

26.12 Revoking Authorization

The Privacy Rule establishes the right for an individual to revoke their authorization for uses and disclosures of PHI for research, in writing, at any time, except to the extent that the covered entity has taken action in reliance on the authorization. [45 CFR 164.508(b)(5)] However, individuals providing authorization should be made aware that revoking authorization does not mean that the individual's PHI may no longer be used in the research or be used or disclosed for other purposes.

At Baptist, research subjects may revoke authorization by notifying the Principal Investigator, as described in the subjects' informed consent/authorization form. When an investigator receives a withdrawal of authorization, s/he should inform the research staff to cease data collection.

A covered entity may continue to use and disclose PHI that was obtained before the individual revoked authorization to the extent that the entity has taken action in reliance on the authorization. When the research is being conducted by the covered entity, the covered entity is permitted to continuing using or disclosing the already obtained PHI to the extent necessary to maintain the integrity of the research (e.g., to account for a subject's withdrawal from a study, to report adverse events, or to conduct an investigation of misconduct). A covered entity may also continue to use the PHI for other activities that are permitted under the Rule without authorization (e.g., health care operations such as QA/QI). Additionally, revoking an authorization does not prevent the continued use or disclosure of PHI by a non-covered entity that had already received it pursuant to the authorization.

26.13 Accounting of Disclosures

The Privacy Rule gives individuals the right to a written accounting of disclosures of PHI made by a Covered Entity or their business associates, including certain disclosures made by researchers who must comply with the rule, in the six years prior to the date on which the accounting is requested (45 CFR §164.528).

It is important to understand the difference between a use and a disclosure of PHI. In general, the

use of PHI means communicating that information within the covered entity. A disclosure of PHI means communicating that information to a person or entity outside the covered entity. The Privacy Rule restricts both uses and disclosures of PHI, but it requires an accounting only for certain PHI disclosures. Researchers with IRB approved protocols where HIPAA Authorization was waived must still comply with HIPAA accounting requirements by tracking certain disclosures of research participant's PHI made by the researchers.

Generally, Accounting of Disclosures are required for:

1. Routinely Permitted Disclosures (e.g., under public health authority, to regulatory agencies, to persons with FDA-related responsibilities) with limited exceptions (e.g., law enforcement, national security, etc.)
2. Disclosures made pursuant to:
    a. Waiver of Authorization
    b. Research on Decedents' Information
    c. Reviews Preparatory to Research unless de-identified

An accounting is not needed when the PHI disclosure is made:

1. For treatment, payment, or health care operations.
2. Under an Authorization for the disclosure.
3. To an individual about himself or herself.
4. As part of a Limited Data Set under a data use agreement.

The Privacy Rule allows three methods for accounting for research-related disclosures that are made without the individual's Authorization or other than a Limited Data Set:

1. A standard approach,
2. A multiple-disclosures approach, and
3. An alternative for disclosures involving 50 or more individuals.

Whatever approach is selected, the accounting is made in writing and provided to the requesting individual. Accounting reports to individuals may include results from more than one accounting method.

If the number of research participants is less than fifty (50), track and maintain a record of any disclosures to include:

1. Patient's name
2. MRN
3. Encounter number
4. Date of service
5. Date of disclosure

6. Name of the person that released the information (if applicable)
7. Name of person/entity who received the information (address if known)
8. Brief description of the purpose that reasonable inform the individual of the basis for the disclosure
9. Brief description of the PHI disclosed
10. Demographic information
11. Clinical information
12. Financial information
13. Entire medical record
14. Medical device information

If there are multiple disclosures of PHI to the same person or entity for a single purpose or under Sections §164.502 or §164.512 of the Privacy Rule each disclosure must include:

1. The date the initial disclosure was made during the accounting period;
2. The name and, if known, address of the person or entity receiving the PHI;
3. A brief description of the PHI disclosed.
4. A brief statement of the reason for the disclosure;
5. The frequency, periodicity, or number of the disclosures made during the accounting period; and
6. The date of the last such disclosure during the accounting period.

In addition, pursuant to 45 CFR§164.512(i), for disclosures of PHI for research purposes without the research participant's authorization and that involve at least 50 records the Privacy Rule allows for a simplified accounting of such disclosures by Covered Entities. Under this simplified accounting provision, Covered Entities may provide individuals with:

1. The name of the protocol or research activity;
2. A plain-language description of the research protocol or activity, purpose of the research, and criteria for selecting particular records;
3. A description of the type of PHI disclosed;
4. The date or period of time during which the disclosure(s) occurred or may have occurred, including the date of the last disclosure during the accounting period;
5. The name, address, and telephone number of the entity that sponsored the research and of the researcher who received the PHI; and
6. A statement that the individual's PHI may or may not have been disclosed for a particular protocol or research activity.

If a health oversight agency or law enforcement official provides a written statement that an accounting would likely impede the agency's activities and specify the time for which a suspension is required, we must honor the temporary suspension.

If the request is made orally: the temporary suspension in the Accounting of Disclosures database is thirty (30) days from the date of the oral statement, unless a written statement is submitted during that time.

For appropriate accounting of PHI disclosures see Baptist Policy S.MI. 4042 – Accounting and Tracking of Disclosures of PHI.

26.14 Security

Baptist has established policies and safeguards to protect patient information and to ensure compliance with federal and state privacy and information security laws and regulations. It is the responsibility of researchers to familiarize themselves with and comply with these policies and safeguards. Researchers must immediately report any known or suspected privacy or security concerns to both the Baptist IRB and Corporate Privacy & Security so that appropriate steps can be taken to assess the situation, protect the information, and comply with regulations.

27 Information Security in Research

Baptist has established standards and safeguards to protect patient's information and to ensure compliance with federal and state information security regulations. It is the responsibility of investigators to familiarize themselves with and comply with these standards.

27.1 Policy

All written paper or printed copies of research data must be stored in a secure location.

The use of personal laptops, desktops, portable/USB drives, and other non-Baptist devices for storage of research data is prohibited. In the instances when a non- Baptist computer or device must be used for the purposes of storing, even temporarily, or transmitting PHI or PII (Personally Identifiable Information) for research, the safeguards of the device must be approved by Baptist Technology Services in coordination with the Corporate Privacy and Security Department. All appropriate agreements must be fully executed prior to use.

Any potential or known breach of a device or of research data must be immediately reported to both the IRB and Corporate Privacy and Security so that appropriate steps can be taken to assess the situation, protect the information, and comply with regulations. Lost or stolen Baptist devices must also be reported to Corporate Privacy and Security.

Provisions for Data Security must be described in applications to the IRB and approved by both Baptist Technology Services and Corporate Privacy and Security and shall be updated as necessary. When information containing direct identifiers such as Social Security numbers or PHI including data considered sensitive is to be transferred outside of the institution, the provisions for data security may be subject to further review and approval by the Corporate Privacy and Security Officer, or designee.

All who participate in the conduct of research at Baptist are required to adhere to all information security polices, including but not limited to:

1. S.AD.1061 Mobile Devices,
2. S.MI.4063 Workstation Usage Guidelines
3. S.MI.4068 Information Access Controls Guidelines, and
4. S.MI.4089 Breach Notification Policy – Unsecured Protected Health Information.

28 Special Topics

28.1 Community Based Research

Community based research (CBR) is research that is based in a community and conducted in collaboration with members of that community. "Community" is often self-defined, but general categories of community include geographic community, a community of individuals with a common problem or issue, or a community of individuals with a common interest or goal.

Where research is being conducted in communities, investigators are encouraged to involve members of the community in the research process, including the design and implementation of research and the dissemination of results when appropriate. The Baptist Clinical Research Institute may be able to assist the investigator in developing such arrangements.

The most significant community involvement is in a subset of CBR called Community Based Participatory Research (CBPR) where there is an equal partnership between the academic investigators and members of a community, with the latter actively participating in all phases of the research process including the design and implementation of research and the dissemination of results when appropriate.

Questions to be considered as CBR studies are developed, and issues that the IRB will consider when reviewing CBR are as follows:

1. How was the community involved or consulted in defining the need for the proposed research (i.e., getting the community's agreement to conduct the research)?
2. How was the community involved or consulted in generating the study research plan?
3. How will the research procedures, including recruitment strategies and consent processes be assessed to ensure sensitivity and appropriateness to various communities (e.g., literacy issues, language barriers, cultural sensitivities, etc.)?
4. How will the community be involved in the conduct of the proposed research?
5. How will community members who participate in the implementation of the research be trained and supervised?
6. How have "power" relationships between investigators and community members on the research team, and in subject recruitment strategies been considered to minimize coercion and undue influence?
7. What are the risks and benefits of the research for the community as a whole?
8. How will boundaries between multiple roles (e.g., investigator, counselor, peer) be maintained, i.e., what happens when the investigator/research staff is the friend, peer, service provider, doctor, nurse, social worker, educator, funder, etc.)?
9. How will the research outcomes be disseminated to the community?

10. Is there a partnership agreement or memorandum of understanding to be signed by Baptist investigator and community partners that describes how they will work together?

When CBR studies are proposed, the above information will be included in the submission materials. When the IRB reviews CBR studies, it will include, either as members or consultants, individuals with expertise in community based research.

28.2 Transnational Research

The IRB will review all transnational research involving human participants to assure adequate provisions are in place to protect the rights and welfare of the participants.

For federally conducted or supported research, approval of research for foreign institutions or sites "engaged" in research is only permitted if the foreign institution or site holds an FWA with OHRP and local IRB review and approval is obtained.

Approval of research is permitted if "the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46." All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate.

Approval of research for foreign institutions or sites "not engaged" in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has an established IRB/EC, the investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/EC has determined that approval is not necessary for the investigator to conduct the proposed research at the site.
- When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials permit the research to be conducted at the performance site.
- IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site's IRB/EC determination, or letter of cooperation, as applicable.

For transnational research, the Baptist IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information will depend on the nature of the study, on the country and on the resources available to the investigator. Where there is a local IRB/EC, the Baptist IRB must receive and review the foreign institution or site's IRB/IEC review and approval of each study prior to beginning the research at the foreign institution or site.

In some circumstances where research may be performed internationally and/or in settings where there are no IRBs/ECs, the Baptist IRB may, prior to approval of the research, require additional verification and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research will be taking place, such as other Baptist investigators with knowledge of the region or a consultant who is an expert on the region. These individuals may either provide a written review of a particular research plan or attend an IRB meeting to provide the Baptist IRB with recommendations based on his or her expertise.

IRB approval to conduct research at the foreign institution or site is contingent upon receiving

documentation of the performance site's IRB/IEC determination, or letter of cooperation, as applicable.

28.2.1 IRB Responsibilities

In addition to standard IRB review, the IRB will consider the following in the review of transnational research:

1. The investigator and research staff are qualified to conduct research in that country, including knowledge of relevant laws, regulations, guidance and customs.

2. The consent process and consent documents are appropriate for the languages of the subjects and communication with the subject population. Arrangements are considered to communicate with the subjects throughout the study (e.g., to answer questions).

3. The IRB considers how modifications to the research will be handled. The IRB and investigators should consider as many contingencies (e.g., survey questions) as possible when research is reviewed and approved.

4. The IRB considers how complaints, non-compliance, protocol/research plan deviations and unanticipated problems involving risks to participants or other are handled.

5. The IRB considers how post-approval monitoring will be conducted.

6. The IRB considers if the investigator has obtained the appropriate host country permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local or tribal). When appropriate, the IRB communicates and coordinates with the local institutions or ethics committees.

7. When applicable, whether the investigator has provided an appropriate plan, and any necessary supporting documentation, to comply with the requirements of country law for investigational articles; and

8. The IRB considers mechanisms for communicating with the investigators and research staff when they are conducting the research in other countries.

28.2.2 Investigator Responsibilities

The investigator conducting transnational research is responsible for:

1. Ensuring that the resources and facilities are appropriate for the nature of the research;
2. Verifying the qualifications of the investigators and research staff for conducting research in the country(ies);
3. Obtaining all appropriate host country approvals and permissions to conduct research (e.g., institutional, governmental or ministerial, IRB, local, or tribal);

4. Complying with the requirements of country law; including, when applicable, requirements for research involving investigational articles and requirements for data management and privacy such as EU GDPR;
5. Ensuring that the consent process and consent document are appropriate for the language(s) of the subjects and the subject population, and that arrangements are made to be able to communicate with subjects throughout the study (e.g., to ask and answer questions);
6. Ensuring that the following activities will occur:
    a. Initial review, continuing review (when required), and review of modifications;
    b. Post-approval monitoring of the conduct of the research in accordance with the plan approved by the IRB; and
    c. Management and reporting of complaints, noncompliance, unanticipated problems involving risk to subjects or others, and other issues that arise in accordance with the research plan, the requirements of the IRB, and the requirements of the locale where the research takes place;
    d. Not relying upon an IRB or EC that does not have policies and procedures for the activities listed above;
    e. Notifying the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins to obtain consent of research participants, etc.); and
7. Ensuring that there are mechanisms for communicating with the IRB when they are conducting the research in other countries;
8. The IRB will not rely on a local ethics committee that does not have policies and procedures for the activities listed above;
9. Investigators will consider how complaints, non-compliance, protocol/research plan deviations and unanticipated problems involving risks to participants or other are communicated to the IRB. It is the responsibility of the Baptist investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins to obtain consent of research participants, etc.);
10. Investigators cooperate with the IRB regarding how and when post- approval monitoring will be conducted;
11. Investigators consider mechanisms for communicating with the IRB when they are conducting the research in other countries.

28.2.3 Consent Documents

The informed consent documents must be in a language understandable to the proposed participants. Therefore, the IRB will review the document, and a back translation of the exact content contained in the foreign language informed consent document which must be

provided by the investigator, with the credentials of the translator detailed in the IRB application. Verification of the back translation should be placed in the IRB file.

28.2.4 Monitoring of Approved Transnational Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review or status report process in accordance with all applicable federal regulations.

When the IRB and a local ethics committee will both be involved in the review of research, there is a plan for coordination and communication with the local IRB/Institutional Ethics Committees (IECs).

The IRB will require documentation of regular correspondence between the Baptist investigator and the foreign institution or site and may require verification from sources other than the Baptist investigator that there have been no substantial changes in the research since its last review.

28.3 Databases, Registries and Repositories

Databases, registries, and biospecimen repositories (all referred to as repositories throughout this section) are used to store data and/or biospecimens for future use.
There are two types of repositories:

- Non-research repositories created and maintained for purposes that are unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance.
- Research repositories created and maintained specifically for research purposes. Such purposes may include databases to identify prospective subjects, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research. Non-research repositories that are altered to facilitate research (e.g., through the addition of data fields not necessary for the core purpose of the repository) are considered research repositories.

28.3.1 Non-research Repositories

Even though repositories were not created for research purposes, they may contain information that is of great interest to researchers. The creation (or operation) of non-research databases or repositories does not involve human subject research and does not require IRB oversight. However, IRB approval is required for the research use of identifiable private information or identifiable human specimens from non-research repositories, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of Baptist that includes the use of coded private information or specimens, must either be submitted for IRB review or for a "Human Subjects Research Determination" (See Section 4).

Researchers submitting an application for research using data or specimens from non-research repositories must describe the source of the data/specimens and any terms, conditions, or restrictions on use. Data/specimens cannot be used for research if the person from whom the data/specimens originated objected to its use for research. Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.

28.3.2 Research Repositories

Research repositories involve three distinct activities:

1. Collection of data/specimens;
2. Storage and management of data/specimens; and
3. Distribution of data/specimens.

<u>Collection</u>

Informed consent and HIPAA authorization (when applicable) must be obtained unless the IRB determines that the criteria for a waiver are satisfied.
Informed Consent information should include:

- A clear description of
  - What data/specimens will be collected;
  - Where the data/specimens will be stored, who will have access, and how the data/specimens will be secured;
  - Whether the data/specimens will be identifiable, coded, or deidentified;
  - The types of research to be conducted and any limitations or restrictions on such; and
  - The conditions under which data/specimens will be released to recipient-investigators
- A statement regarding future withdrawal of the data from the study (i.e., state whether subjects may, in the future, request that their data be destroyed or that all personal identifiers be removed from data and how to make such a request)
- When appropriate, the plan for management of incidental findings and sharing of results

Storage and Management

Repositories should have written policies describing:

- The conditions under which data/specimens will be accepted (e.g., inclusion criteria)
- Informed consent
- IRB review
- The sources of data/specimens
- Whether data/specimens will be identifiable, coded, or de-identified, and, if coded, management of the linkage key; and
- Physical and procedural mechanisms for the secure receipt, storage, and distribution of data/specimens

Distribution

Repositories should have written policies describing:

- How data/specimens may be requested and by whom
- Any requirements associated with a request for data/specimens (e.g., verification of IRB approval or that approval is not required)
- Any limitations or restrictions on how data/specimens may be used

- Whether released data/specimens will be identifiable, coded, or de-identified, and, if coded, any circumstances under which recipient investigators will have access to or be provided with the key or other means to re-identify; and
- Agreements with recipient investigators specifying the terms of use.

28.3.3 IRB Oversight

IRB approval is required for the establishment and operation of a research repository when the data/specimens that are accessed, received, stored, or distributed are identifiable. In general, private information or specimens are considered individually identifiable when the identities of the subjects are known to investigators/repository operators or when the data/specimens can be linked to specific individuals either directly or indirectly through coding systems.

Separate IRB approval is required for the use of data/specimens from a repository when the recipient investigator(s) know or may readily ascertain the identity of individual subjects, and, regardless of identifiability, when specimens will be used to evaluate the safety or effectiveness of a medical device. Research under the auspices of Baptist that includes the use of coded private information or specimens, must either be submitted for IRB review or for a "Human Subjects Research Determination" (See Section 4). The only exception to this policy is when the coded private information or specimens are to be obtained from an IRB-approved repository and the rules of that repository forbid the release of identifiable information, the release of the key to the code or other means that would allow re-identification, or the release of sufficient information that investigators could readily ascertain the identity of subjects.

28.4 Certificates of Confidentiality

Note: As of June 11, 2025, the NIH Certificates of Confidentiality (CoC) system is temporarily unavailable while undergoing renewal of its Paperwork Reduction Act (PRA) approval. Currently, NIH cannot accept submissions to the CoC system or Institutional Official verifications. An update will be provided by July 2025. Also, NIH may reject CoC applications for research topics that are not consistent with agency priorities.

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized below.

CoCs are obtained as follows:

- CoCs are issued automatically when research is conducted or supported by NIH and falls within the scope of the NIH policy.
- CoCs are issued automatically when research is conducted or supported by the CDC and involves the collection of identifiable, sensitive information.
- CoCs are issued automatically when research is funded by the FDA in whole or in part and involves the collection or use of identifiable, sensitive information as defined in 42 U.S.C. 241(d).
- CoCs are issued automatically when research is conducted or supported by BARDA and falls within the scope of the BARDA policy.
- CoCs are issued automatically when research is conducted or supported by HRSA and falls within the scope of the HRSA policy.
- Other agencies like SAMHSA and IHS still require a CoC application for research that they fund. NIH maintains a list of CoC Coordinators and Contact Information for Non-NIH HHS Agencies that Issue Certificates.
- Research that is not supported by NIH, CDC, BARDA, HRSA, SAMHSA, IHS, or FDA may still benefit from the protections afforded by CoCs through successful application to the NIH, FDA, or other authorized Federal agencies or departments.
- Research that is not supported by NIH, CDC, or FDA may still benefit from the protections afforded by CoCs through successful application to the NIH, FDA, HRSA, SAMHSA, or other authorized Federal agencies or departments.

Additional information about CoCs and the application process for research not covered by the NIH policy is available on the NIH CoC Website. Information about discretionary CoC's issued by FDA is available in the FDA guidance document: Certificates of Confidentiality.

28.4.1 Definitions

Identifiable, sensitive information means information that is about an individual and that is

gathered or used during the course of biomedical, behavioral, clinical, or other research and

1. Through which an individual is identified; or

2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

28.4.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

2. To any other person not connected with the research, unless:

    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in "1" above;

    b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;

    c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or

    d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to

protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about himself or herself collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

28.4.3 NIH and CDC

The NIH Policy on CoCs applies to "all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information" that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to "CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d)."

The BARDA Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by BARDA, whether supported through contracts, cooperative agreements, grants, other transaction awards, or research ("Awards") that collects or uses Covered Information"* (i.e., identifiable, sensitive information) that was commenced on or after July 17, 2023.

The HRSA Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by HRSA, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by HRSA staff, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC's requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.

NIH and CDC expand upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);
- Research involving the collection or use of biospecimens that are identifiable to

an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;

- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, **regardless of whether the data is recorded in such a manner that human subjects can be identified, or the identity of the human subjects can readily be ascertained;** or

- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

Certificates of Confidentiality (CoCs) issued for NIH, CDC, HRSA, or BARDA funded human subject research do not need to be extended or amended while the research remains funded.

If the NIH, CDC, HRSA, or BARDA funding ends, the study will no longer be deemed issued a CoC. While CoC protections remain in perpetuity for already collected or used information, a new CoC will need to be obtained in order to cover any new data collected from already enrolled participants or any new participants. In this case, investigators should request a new CoC following the process for non-federally funded research.

28.4.4 FDA

The FDA requires, as a term and condition of all FDA funding and grant awards, compliance with the requirements of 42 U.S.C. 241(d) when research is funded in whole or in part by the FDA and involves the use or collection of identifiable, sensitive information. Certificates are deemed issued through FDA funding/award terms and conditions and are not issued as a separate document.
Investigators and institutions are responsible for determining when research with FDA support is covered by a CoC and for ensuring compliance with the requirements of 42 U.S.C. 241(d). Awardees are expected to ensure that any investigator or institution not funded by FDA who receives a copy of identifiable, sensitive information protected by these requirements, understand they are also subject to the requirements of 42 U.S.C. 241(d). Awardees are also responsible for ensuring that any subrecipient that receives funds to carry out part of the FDA award involving a copy of identifiable, sensitive information protected by these requirements understand they are also subject to subsection 42 U.S.C. 241(d).

When research is not funded by the FDA but involves an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA. Information about discretionary CoC's issued by FDA is available in the FDA guidance document: Certificates of Confidentiality.

Mandatory Certificates of Confidentiality (CoCs) issued for FDA funded human subject research do not need to be extended or amended while the research remains funded. CoC protections remain in perpetuity for already collected or used information; however, a new CoC will need to be obtained in order to protect the privacy of any new human subject research participants from whom identifiable, sensitive information is being collected or used in furtherance of the research, or for new data collected after FDA funding has ended. Researchers could seek a discretionary CoC for such information and data.

28.4.5 NIH, CDC, BARDA, HRSA and FDA CoC Determination

At Baptist, Grants Management staff will, in consultation with the investigator(s) (or Program or Project Director, if applicable), determine if the NIH, BARDA or HRSA policies or CDC or FDA requirements apply to research with NIH, BARDA or HRSA, CDC or FDA involvement or support. The questions outlined in the NIH, BARDA, or HRSA policies and CDC requirements will be used to guide the analysis for research conducted or supported by NIH, BARDA, HRSA, and CDC. The definitions and text of 42 U.S.C. 241(d) will be used to guide the analysis for research supported by FDA funding/awards. When it has been determined that the NIH, BARDA or HRSA policies or CDC requirements do not apply, investigators (or Program or Project Directors, if applicable) are responsible for consulting with SPA whenever they are proposing changes to the supported activity that may impact or change the analysis.

The NIH, BARDA, and HRSA policies and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act. Likewise, FDA requires awardees ensure that recipients of identifiable, sensitive information protected by an FDA CoC understand that they are also subject to the requirements of 42 U.S.C. 241(d).

28.4.6 Application Procedures for Research Not Automatically Issued a CoC

Any person engaged in human subjects research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH, an investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When a researcher is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed because the Privacy Certificatemakes identifiable data immune from any legal action.

When research is not funded by the FDA but involves “the use or study of a product subject to FDA’s jurisdiction and subject to FDA’s regulatory authority” (e.g., a clinical investigation of a drug, device, or biologic), the sponsor or sponsor-investigator can request a discretionary CoC from the FDA. When FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMHSA or IHS. For research that is supported by SAMHSA or IHS, researchers must contact the respective CoC Coordinator to request a SAMHSA-issued or IHS-issued CoC. Information about the SAMHSA CoC application process, including the extension of protections and amendments to certificates can be found at https://www.samhsa.gov/grants/gpra-measurement-tools/certificate-confidentiality. The IHS CoC contact can be found on the NIH Coc website at CoC Coordinators and Contact Information for Non-NIH HHS Agencies that Issue Certificates.

For more information, see the NIH CoC Website.

28.4.7 IRB Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted or is pending. When the CoC application is in process or pending, the IRB may condition final approval upon its receipt.

For studies that are already underway, investigators must submit a Modification Request to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH, FDA, BARDA, or HRSA policies or CDC requirements.

When reviewing research under a CoC, the Baptist IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.

28.5 Mandatory Reporting

While any person may make a report if they have reasonable cause to believe that a child or elder was abused or neglected, Tennessee law mandates that certain persons who suspect child or elder abuse or neglect report this to the Division of Child Protection and Permanency or Adult Protective Services.

Baptist policy requires the solicitation of informed consent from all adult research subjects and, where appropriate, also requires the assent from children involved as research subjects, in addition to the informed consent and permission of their parents. In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of abuse or neglect.

Investigators should consult these sources to determine if potential subjects should be advised of mandatory reporting requirements during the informed consent process.

28.6 Students and Employees as Subjects

When students and/or employees are being recruited as potential subjects, investigators must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be primary and without undue influence on their decision. Investigators must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision.

To minimize coercion, investigators must avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. In these latter situations, investigators must solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own. When entering a classroom to recruit students and conduct research, e.g., administer a survey, investigators must do so at the end of the class period to allow non-participating students the option of leaving the classroom, thereby alleviating pressure to participate.

28.7 Student Research

Human Subject Research and Course Projects: Learning how to conduct ethical human subject research is an important part of a student's educational experience. Research activities that are designed as part of a course requirement for purposes of learning experience only and are not "designed to develop or contribute to generalizable knowledge" may not require IRB review and approval if all of the following conditions are true:

1. Results of the research are viewed only by the course instructor for teaching purposes and discussed within the classroom for teaching and learning purposes;
2. Results of the research are not made public through presentation (outside of the classroom) and are not published in paper or electronic format (e.g., cannot be made available on the internet, cannot be published in a journal, etc.);
3. Research procedures are no more than minimal risk;
4. Vulnerable populations are not targeted (e.g., children under age 18, prisoners, persons who are cognitively impaired, etc.);
5. Data collected are recorded in such a manner that the subjects are not identifiable (images in videotapes and photographs and voices on audiotape are identifiable); and,
6. When appropriate, an informed consent process is in place.

28.7.1 Responsibility of the Course Instructor:

The course instructor is responsible for communicating to the students the ethics of human subject research, for ensuring the protection of human subjects (including a process is in place for obtaining voluntary informed consent from research subjects when appropriate), and for monitoring the students' progress.

When designing a project, students should be instructed on the ethical conduct of research and on the preparation of the IRB application when such is required. In particular, instructors and students should:

1. Understand the elements of informed consent;
2. Develop appropriate consent documents;
3. Plan appropriate strategies for recruiting subjects;
4. Identify and minimize potential risks to subjects;
5. Assess the risk-benefit ratio for the project;
6. Establish and maintain strict guidelines for protecting privacy and confidentiality;

and,

7. Allow sufficient time for IRB review (if necessary) and completion of the project.

In making a determination of whether or not a class research project requires IRB review, the instructor is encouraged to contact the IRB office for assistance.

28.7.2 Individual Research Projects Conducted by Students

Independent study projects, senior theses, undergraduate research projects, Masters and advanced degree research, and similar exercises must be independently submitted for IRB review. It is important to keep in mind that any human subject research activity that will ultimately contribute to part or all of a thesis, dissertation, or other type of publication or presentation must go through the IRB review process prior to enrolling subjects and collecting data. IRB review/approval cannot occur after a study has begun. Students and advisors should contact the IRB Office with any questions.

28.7.3 Independent Study, Theses and Dissertations

These research activities are considered to meet the federal definition of human subject research and must be independently submitted to the IRB by the student-investigator. However, when students conduct research as part of a course of study, a faculty member ultimately is responsible for the protection of the subjects, even if the student is the primary investigator and actually directs the project. Advisers assume the responsibility for students engaged in independent research, and instructors are responsible for research that is conducted as part of a course.

Students may not serve as principle investigators. They must have a faculty sponsor who fulfills the principle investigator eligibility criteria and who will serve as principle investigator and faculty advisor on the study.

28.8 Research Involving or Generating Genetic Information

Research that generates or uses genetic information may create special risks to human subjects and their relatives. These involve medical, psychosocial, legal and economic risks, such as the possible loss of privacy, insurability, and employability, and may result in stigmatization and discrimination. Information about one's own genetic make-up may also provide information about family members.

In studies involving genetic testing or analysis of genetic information, several questions should be addressed to ensure that potential risks are well understood and that the rights and interests of subjects and their family members are carefully considered and planned for. For example:

1. Is the testing intrinsic to the study? If not, has participation in the genetic testing component been provided as an opt-in?
2. Will test results be given? Is there an appropriate plan for return of results?
3. Will the subject or family member be provided the option to receive or not receive results?
4. How will this decision be recorded?
5. Could the results provide information about individual disease risk? Disease risk for family members?
6. Could other clinically relevant information or incidental findings be uncovered by the study? Is there a plan for the management of such findings?
7. Will testing that could produce clinically relevant information occur in a CLIA-certified lab? If not, are there tests available that could validate or support findings?
8. Could a change in a family relationship be disclosed, such as mistaken paternity?
9. Could/will the research provide information about the origins, ancestry, or natural history of families, indigenous peoples, tribal populations, or other populations? What are the possible risks?
10. Could/will the research generate information that could place subjects or family members at risk or be stigmatizing?
11. Could/will the research generate information of other value or importance to subjects/families?
12. Are there any practical limitations on the subject's right to withdraw from the research, withdraw data, and/or withdraw biological materials (e.g., specimens, cell lines, extracted genomic DNA)? If so, what are they?

13. How will the information and/or biological materials be protected and who will have access?

14. What is the potential for re-identification of individual subjects (e.g., through the combination of their genetic information and/or materials with other sources of information (e.g., public records))? What measures can be taken to mitigate these risks?

15. Is a Certificate of Confidentiality (CoC) in place or should one be considered?

16. Will the specimens, cell lines, or genetic information be stored and/or made available for future research? Is this provided as an opt-in when not intrinsic to the study?

Investigators should carefully consider the above and other factors relevant to their specific study when developing the protocol, consent process, and consent form. The President's Bioethics Commission, the National Academies of Sciences, Engineering, and Medicine, and others have produced reports, recommendations, and materials that investigators and the IRB may find helpful in protocol development and review, including:

- Returning Individual Research Results to Participants: Guidance for a New Research Paradigm
- Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts
- Privacy and Progress in Whole Genome Sequencing
- Genetics Research and American Indian and Alaska Native Communities
- National Human Genome Research Institute:
    - Human Subjects Research in Genomics
    - Return of Research Results
    - Data Sharing and Privacy
    - Informed Consent for Genomics Research

In addition to the ethical considerations, investigators must ensure that research involving genetic testing or use of genetic information is consistent with applicable law (e.g., GINA, HIPAA, EU GDPR, state law) and policy (e.g., NIH).

28.9 Genetic Information Nondiscrimination Act (GINA)

GINA generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against individuals based on their genetic information. This law protects individuals, including research subjects, in the following ways:

- Health insurance companies and health plans are generally prohibited from requesting or requiring genetic information of an individual or their family members, including genetic information generated from research;
- If health insurance companies and health plans do receive such genetic information, they may not use it to make decisions regarding coverage, rates, or preexisting conditions; and
- Employers with 15 or more employees generally may not use genetic information for hiring, firing, promotion, or other decisions regarding terms of employment.

GINA's protections do not extend to life insurance, disability insurance, or long-term care insurance.

GINA defines genetic information as information about:

- An individual's genetic tests;
- Genetic tests of an individual's family members;
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
- The manifestation of a disease or disorder in an individual's family members (family history); or
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

GINA includes a "research exception" that allows health insurers and health plans who are engaged in research to request, but not require, that an individual undergo a genetic test so long as certain requirements are satisfied. Additional information on GINA and this exception are available on this OHRP website.

The Baptist IRB will consider the protections and limitations of GINA when it assesses the risks of research generating or using genetic information and the adequacy of the measures to protect privacy and maintain confidentiality. Generally, the IRB will also require that the protections and limitations of GINA are disclosed in the consent process when applicable.

28.10 Genomic Data Sharing (GDS)

NIH has purposely set a higher standard than is required by regulation: "…the NIH GDS Policy requires that informed consent be obtained for the future research use and broad data sharing of de-identified data from biospecimens created or collected after January 25, 2015 (the effective date of the GDS Policy). While the Common Rule does not require informed consent for research with de-identified biospecimens or cell lines, the GDS Policy establishes expectations and protections beyond those of both the current, and the revised Common Rule because the evolution of genomic technology and analytical methods may raise the risk of potential re-identification.")

Baptist complies with the NIH GDS Policy, which allows for "broad and responsible sharing of genomic research data", via submission of said data into an NIH-designated data repository. The intent of NIH's policy is to speed discoveries to diagnose, treat, and prevent disease. To ensure consistency in the protection of human subjects, Baptist applies the NIH principles for informed consent and for a genomic data sharing plan to all research that involves or contemplates genomic data sharing.

The NIH policy applies to grant activities requesting support from NIH for research involving the generation of large-scale human (and/or non-human) genomic data, regardless of funding level, such as:

- Research project grants (Rs);
- Program projects (Ps) and SCORs (Ss);
- Cooperative agreements for research (Us);
- Individual career development awards (Ks) that include a research component;
- S activities that include a research component; and
- All other activities that include a research component.

Also covered under this policy is research involving data derived from these activities for subsequent research. All basic and clinical research, including clinical trials, supported by NIH that involves the generation or use of large- scale genomic data fall within the scope of the policy.

The policy does not apply to:

- Institutional training grants (T32s, T34s, T35s, and TL2s);
- K12 career development awards (KL2s);
- Individual fellowships (Fs);
- Resource grants and contracts (Ss);

- Linked awards derived from previously reviewed applications (KL1, KL2, RL1, RL2, RL5, RL9, TL1, UL1);

- Facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

Because of the potential for re-identification of genomic data, Certificates of Confidentiality (CoCs) are automatically issued by the NIH for any research it supports, in part or in whole, that involves "the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46)." Research covered by the NIH policy and/or the underlying PHS Act is protected by the CoC in perpetuity; as such any downstream recipients of such information must comply with the requirements of the PHS Act.

A.

Investigators without NIH support who intend to submit genomic data to a NIH repository are encouraged to obtain a CoC. (Optional): Investigators conducting research generating or using genomic data are encouraged to obtain a CoC when one is not already in place (e.g., for downstream use of data that was collected under a CoC.

28.10.1 Definitions

Genomic data: information derived from study of an organism's genome, i.e., the set of DNA (including all the genes within) in every cell that provides all of the information needed to build and maintain that organism.

Genomic Summary Results (GSR): GSR (also referred to as "aggregate genomic data" or "genomic summary statistics") are results from primary analyses of genomic research that convey information relevant to genomic associations with traits or diseases across datasets rather than associations specific to any one individual research participant (e.g., genotype counts and frequencies; allele counts and frequencies; effect size estimates and standard errors; likelihood; and p-values). **Sensitive GSR** refers to GSR where the privacy risks may be heightened for study populations (e.g., populations from isolated geographic regions or with rare traits) or the study populations may be more vulnerable to group harm (e.g., because the data includes potentially stigmatizing traits). Information regarding NIH's updated policy on the access, use, and management of GSR may be found here: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-023.html

Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Examples of genomic research projects that are subject to the Policy and the timeline for submission and sharing of data from such projects may be found here: https://osp.od.nih.gov/wp-content/uploads/Supplemental_Info_GDS_Policy.pdf

NIH-Designated Data Repository: any data repository maintained or supported by NIH either directly or through collaboration. Examples of such repositories is available here: https://osp.od.nih.gov/scientific-sharing/data-repositories-and-trusted-partners/. Data may be unrestricted or controlled access:

- **Unrestricted-Access ("Open Access"):** data are publicly available to anyone (e.g., The 1000 Genomes Project). Non-sensitive GSR are made available through unrestricted access.
- **Controlled-Access:** the data are available to an investigator for a specific project only after the investigators and institution certify to abide by specified terms and conditions and NIH has approved the use. Sensitive GSR are made available through controlled access.

28.10.3 IRB Submissions and GDS

For any cell lines created or specimens to be collected, analyzed, and shared subject to the GDS Policy, the IRB expects that informed consent will be obtained from the research subject for the future research uses and broad sharing of data required under the policy, including GSR. This is the case even if the specimens or cell lines are de-identified. If there are compelling scientific or legal reasons that necessitate the use of genomic data from cell lines or clinical specimens that lack consent for research use and data sharing, investigators will need to provide a justification in the funding request to NIH for their use. The funding NIH institute/center will review the justification and decide whether to make an exception to the consent expectation. Exceptions from the NIH are not required if only some participants decline to consent to broad sharing, rather an exception request must be granted by NIH for research when consent for broad sharing has not or will not be sought.

Subjects asked to allow for future research uses and broad sharing of their genomic data have the ability to decline, and still remain in the research (however their data cannot be placed into a repository or otherwise broadly shared). The only exception to this is when sharing of the data is intrinsic to the study (e.g., the purpose of the study is to establish a repository for sharing biological specimens and/or data for future research).

Sample consent language for studies subject to GDS is available in the consent template, from the HRPP/IRB Office. NIH and NHGRI also provides guidance and resources to assist in the development of appropriate consent forms for research involving or generating genetic or genomic data.

Applications to the Baptist IRB should include information about the proposed generation or use of genomic data including, as applicable:

- Whether the research will generate or use data subject to the NIH GDS policy;

- The name of the NIH data repository/database, or other repository or database, that

data will be submitted to or acquired from;

- Whether the data is or should be classified as restricted access or unrestricted access;
- Whether the data is or should be classified as sensitive (e.g., studies involving populations from isolated geographic regions or with rare traits, studies that include data on potentially stigmatizing traits, etc.)
- Whether there are any data use limitations or modifiers (e.g., use limited to a specific disease, restricted to not-for-profit organizations, IRB approval requirement, etc.);
- The plan for informed consent and the proposed consent language; and
- A copy of the genomic data sharing plan.

The IRB will review the proposal for genomic data sharing or subsequent use of such genomic data in accordance with the criteria for approval of research and the guidelines for IRBs provided by NIH.

When Baptist is responsible for NIH Institutional Certification (see below), the IRB review will specifically address the required assurances outlined on the Extramural Institutional Certification. When appropriate, if the IRB is unable to confirm that a certification element is satisfied (e.g., because the IRB has not yet granted final approval), Provisional Institutional Certification will be provided.

28.10.4 Grant Applications and GDS

Investigators planning to apply to NIH for research that will generate large- scale human genomic data as defined above should contact the appropriate NIH Program/Project officials to discuss expectations and timelines for complying with this policy. Along with the grant, the following will need to be submitted:

- Notification in a cover letter of the intent to generate large-scale human genomic data
- A genomic data sharing plan, within the grant's resource sharing plan section (NIH guidance on these plans is available here: https://osp.od.nih.gov/wp-content/uploads/NIH_Guidance_Developing-GDS_Plans.pdf)
- Institutional Certification from the Office of Sponsored Programs (templates available here: https://osp.od.nih.gov/scientific-sharing/institutional-certifications/). Certification must be provided for all sites contributing samples. If more than one site is contributing samples, the primary site may submit one certification on behalf of all collaborating sites (or each site may provide their own certification if this is the site's preference). This certification assures that:

- The data submission is consistent, as appropriate, with applicable national, tribal, and state laws and regulations as well as relevant institutional policies;
- Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated within the certification;
- The identities of research participants will not be disclosed to the repositories;
- An IRB and/or Privacy Board has reviewed the investigator's proposal for data submission and assures that:
    - the protocol for the collection of genomic and phenotypic data is consistent with 45 CFR 46;
    - data submission and subsequent data sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
    - consideration was given to the risks to individual participants and their families associated with data submitted to the repositories and subsequent sharing, including unrestricted access to GSR; and
    - the investigator's plan for de-identifying datasets is consistent with the standards outlined in the NIH Genomic Data Sharing (GDS) Policy (See section IV.C.1).

- In situations where the sharing of human data is not possible (i.e., the Institutional Certification criteria cannot be met), a justification is required to explain why these data cannot be shared, and an alternative data sharing plan will need to be provided. Exceptions to NIH expectations for data submission to an NIH-designated data repository will be considered on a case-by-case basis by the NIH funding Institute or Center (IC).

Investigators who wish to use controlled-access human genomic data from NIH-designated data repositories should briefly address their plans for requesting access to the data and state their intention to abide by the NIH Genomic Data User Code of Conduct in the Research Plan of the application. The code of conduct is available here: https://osp.od.nih.gov/wp-content/uploads/Genomic_Data_User_Code_of_Conduct.pdf. Access to controlled-access data is dependent on an approval process that involves the relevant NIH Data Access Committee(s). Applicants may wish to secure access to the data prior to submitting their application for NIH support. Secondary users of controlled-access data are not expected to deposit their findings into NIH-designated data repositories, unless appropriate.

Investigators who wish to use/download data NIH unrestricted-access repositories, including non-sensitive GSR, should use the data to promote scientific research or health; and should not use the data to re- identify individuals or generate information that could allow

participant's identities to be readily ascertained, and, in all oral and written presentations, disclosures, or publications, acknowledge the specific dataset or accession numbers and the repository through which the data were accessed.

Procedures for submitting data into, or requesting access for data from an NIH-designated repository, are available here: https://osp.od.nih.gov/scientific-sharing/researchers-institutional- certifications/.

28.11 Case Reports

Definitions:

Single Case Report. The external reporting (e.g., publication, poster or oral presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

Case Series (up to four patients). The external reporting (e.g., publication, poster or oral presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). Case series usually contain detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

In general, an anecdotal report on one or a series of patients seen in one's own practice and a comparison of these patients to existing reports in the literature is not research and does not require IRB approval. Going beyond one's own practice to seek out unique cases and report cases seen by other clinicians creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge and therefore is considered research and would require IRB approval.

28.12 Research Supported by the Department of Defense (DoD)

The U.S. Department of Defense (DoD) is a signatory to the Common Rule with regulations equivalent to 45 CFR 46 published under 32 CFR 219. Research conducted or supported by DoD is subject to additional requirements for investigators and for reviewing IRBs. These requirements are outlined in this section.

DoD support of a study includes funds or assistance by the DoD through a grant, contract, or similar agreement, and also includes provision of assistance such as facilities, equipment, personnel (investigators or other personnel performing tasks identified in the research protocol), access to or information about DoD-affiliated personnel for recruitment, or data or specimens.

The Baptist IRB will review DoD research in accordance with the Common Rule (at 32 CFR 219) and applicable DoD requirements, including:

- DoD Instruction (DoDI) 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-supported Research"
- Subparts B, C, and D of 45 CFR 46 with modifications as described in DoDI 3216.02
- Title 10 United States Code Section 980 (10 U.S.C. 980), "Limitation on Use of Humans as Experimental Subjects"
- DoDI 3210.7, "Research Integrity and Misconduct"
- DoDI 6200.2, "Application of Food and Drug (FDA) Rules to Department of Defense Force Health Protection Programs"
- Any additional applicable requirements from the respective DoD component (e.g., Army, Navy, Air Force, Marine Corps, Defense Intelligence Agency, National Security Agency, etc.)

It is the responsibility of the PI to ensure compliance with DoD requirements for human subject research. IRB staff, chairs and members will use these SOPs, DoDD 3216.02, a DoD Reviewer Checklist, and any relevant DoD Component-specific instructions or materials to guide the IRB review and oversight of DoD research.

28.12.1 Activities Not Considered Human Subjects Research ('excluded activities')

In addition to the activities deemed "Not Research" in the 2018 Common Rule, the following activities conducted or supported by the DoD are not considered Human Subjects Research (HSR):

- Activities carried out solely for purposes of diagnosis, treatment, or prevention of injury and disease under force health protection programs of DoD, including health surveillance pursuant to 10 U.S.C. 1074f, and the use of medical products consistent with DoDI 6200.02.

- Health and medical activities as part of the reasonable practice of medicine or other health professions undertaken for the sole purpose of diagnosis, cure, mitigation, treatment, or prevention of disease in a patient.
- Activities performed for the sole purpose of medical quality assurance (see 10 U.S.C. 1102, and DoDI 6025.13).
- Activities that meet the definition of operational test and evaluation as defined in 10 U.S.C 139(a)(2)(A).
- Activities performed solely for assessing compliance, including occupational drug testing, occupational health and safety reviews, network monitoring, and monitoring for compliance with requirements for protection of classified information.
- Activities, including program evaluation and surveys, user surveys, outcome reviews, and other methods, designed solely to assess the performance of DoD programs where the results are only for the use of government officials responsible for the operation or oversight of the program being evaluated.

28.12.2 Single (sIRB) Mandate

Effective 20 January 2020, any institution located in the U.S. that is engaged in multi-site cooperative human subjects research must rely upon approval by a single IRB for that portion of the research that is conducted in the U.S. unless the relevant DoD Component Office of Human Research Protections (COHRP) determines and documents that use of a single IRB is not appropriate for the particular context of the proposed research. Studies already in progress before January 20, 2020 are not required to transition to a single IRB.

When any institution relies upon another institution's IRB for DoD-covered research, there must be a written agreement defining the responsibilities and authorities of each organization in complying with the terms of each institution's Federal Assurance and DoDD 3216.02. When appropriate, the lead institution or reviewing IRB may take responsibility for required DoD reporting.

When a DoD institution is engaged in a DoD-covered research study and is relying upon the Baptist IRB, each of the following conditions must be met:

- Each institution engaged in non-exempt human subjects research must have a current FWA.
- The Baptist IRB must be registered in accordance with 45 CFR 46 Subpart E.
- The DoD institution must review the protocol to ensure that all applicable local and DoD requirements are addressed.
- The DoD institution and Baptist have a written reliance agreement defining the responsibilities and authorities of each institution in complying with all legal requirements, including that the IRB will apply the DoD requirements outlined in DoDI 3216.02, including the institutional responsibilities outlined in Section 3.6(b).

- If the research is classified, the Component OHRP must approve the agreement to rely on Baptist's IRB.

The primary awardee (lead institution) of a DoD-conducted or supported research proposal that includes a multi-site, cooperative effort is responsible for developing a plan for coordinating all collaborating sites' reliance on a single IRB for DoD-supported multi-site cooperative research.

28.12.3 Education and Training

All personnel involved in the conduct of DoD research must complete initial and continuing education in the protection of human subjects as described in this manual (see Section 3). Personnel must also familiarize themselves with DoD's specific requirements by reviewing these SOPs, DoDI 3216.02, and any relevant materials specific to the DoD component. The DoD component may require additional education and/or certification to ensure that personnel are qualified to perform the research.

28.12.4 Selection of Subjects

The selection of human subjects in DoD-conducted or supported research must comply with Section 252 (Inclusion of Women and Minorities in Clinical Research Projects) of the National Defense Authorization Act for Fiscal Year 1994 (Public Law 103-160), with respect to gender, minority participation, and membership in the Armed Services unless this requirement is waived by the Secretary of Defense, or, when delegated, by the relevant DoD Component.

28.12.5 Evaluating Risk

Minimal Risk is defined in the Common Rule (at 32 CFR 219) as meaning 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 examinations or tests.

However, per DoDI 3216.02, this definition may not be interpreted to include the inherent occupational risks that certain subjects face in their everyday life, such as those:

- Encountered by Service members, law enforcement, or first responders while on duty.
- Resulting from or associated with high-risk behaviors or pursuits.
- Experienced by individuals whose medical conditions involve frequent tests or constant pain.

28.12.6 Informed Consent/HIPAA Authorization

28.12.6.1 Additional Consent/Authorization Elements

When consent is to be obtained from subjects in DoD-conducted or supported research, the following additional information should be provided to potential subjects in the consent document when applicable unless the requirement is waived by the DoD:

- A statement that the DoD or DoD component is conducting or supporting the research.
- A statement that representatives of the DoD are authorized to review research records.
- If the research involves DoD-affiliated personnel as subjects and includes any risks to their fitness for duty (e.g., health, availability to perform job, data breach), the consent must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.
- If the research involves DoD-affiliated personnel as subjects, the consent must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.
- If a Certificate of Confidentiality (CoC) is in place, exceptions to the CoC must be listed.
- If the research is greater than minimal risk and is conducted by the DoD, the explanation regarding the availability of compensation and medical treatments for research-related injuries must include a statement that subjects may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, in accordance with 32 CFR 108. This eligibility for health care services extends beyond subjects' participation in the study to such time after the study has ended.

When HIPAA authorization is to be obtained, the authorization should include a statement that protected health information may be disclosed to representatives of the DoD.

When a DoD component will acquire data under a pledge of confidentiality for exclusively statistical purposes, the data may not be disclosed in identifiable form for any other purpose unless consent is obtained.

28.12.6.2 Limitation of Waivers and Alterations of Informed Consent

10 U.S.C. 980 addresses requirements related to informed consent, or the waiver thereof, for research supported by DoD funds that involves a human being as an experimental subject.

Per DoDI 3216.02, research involving a human being as an experimental subject is defined as:

"An activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as an experimental subject is a subset of research involving human subjects."

This definition relates only to the application of 10 U.S.C. 980 (see above); it does not affect the application of the Common Rule at 32 CFR 219.

When Baptist engages in non-exempt research involving a human being as an experimental subject that is supported or conducted by the DoD, informed consent must be obtained in advance from the experimental subject or their LAR if the subject cannot consent. If consent is to be obtained from a LAR, the research must be intended to be beneficial to the subject.

The requirement for advanced informed consent may be waived (e.g., for planned emergency research) by the DoD Office for Human Research Protections (DOHRP) or its delegate if the following conditions are met:

- The research is to advance the development of a medical product necessary to the DoD;
- The research may directly benefit the individual experimental subject; and
- The research is conducted in compliance with all other applicable laws and regulations.

Investigators are responsible for ensuring that all DoD requirements are met before initiating the research.

If the research involves no more than minimal risk, the IRB may alter or waive other required elements of informed consent so long as it still preserves informed consent of the subject (i.e., the consent indicates the subject's participation in the research is completely voluntary and includes the requirement that the subject is informed of research risks).

28.12.6.3.Posting of Clinical Trial Informed Consent Forms

When DoD-conducted or supported research is a clinical trial as defined at 32 CFR 219.02(b), the DoD Component Office for Human Research Protections (COHRP) has the authority to review and determine appropriate redactions prior to posting informed consent forms pursuant to 32 CFR 219.116(h).

28.12.7 Additional Protections for Human Subjects

28.12.7.1 Pregnant Women, Fetuses, or Neonates as Subjects

Non-exempt research involving pregnant women, fetuses, or neonates as subjects must meet the requirements of Subpart B of 45 CFR 46, with the following modifications:

- The applicability of Subpart B is limited to research involving pregnant women in research that is greater than minimal risk and that includes interventions or invasive procedures involving
  - The woman or the fetus; or
  - Fetuses or neonates as subjects.

- For purposes of applying Subpart B, the phrase "biomedical knowledge" is replaced with "generalizable knowledge."
- Fetal research must comply with 42 U.S.C 289g – 289g-2.

  Explicit written approval is required from the DOHRP before the research begins for research that would not otherwise be approvable under Subpart B but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.

28.12.7.2 Prisoners as Subjects

Research involving prisoners as subjects must meet the requirements of Subpart C of 45 CFR 46, with the following modifications:

- In addition to the four allowable categories of research involving prisoners in Subpart C, two additional categories are allowable:
  - Certain epidemiological research in accordance with the HHS waiver published in Federal Register, Volume 68 pages 36929-36931 that meets the requirements of 45 CFR 46 Subpart C, DoDD 3216.02, and other applicable requirements.
  - Research that would meet the criteria for exemption described at 32 CFR 219.104, but such research must first be approved by an IRB and meet the requirements of 45 CFR 46 Subpart C, DoDD 3216.02, and other applicable requirements.
- When a previously enrolled human subject becomes a prisoner, and the research was not previously approved for the inclusion of prisoners:
  - The PI must promptly notify the IRB.
  - Baptist must notify the HRPO and other federal agencies (if required).
  - The HRPO must concur with the IRB before the subject can continue to participate while a prisoner.

28.12.7.3 Children as Subjects

Research involving children as subjects must meet the requirements of Subpart D of 45 CFR 46 and 21 CFR 50.54, if applicable**.**

28.12.7.4 Detainees or Prisoners of War

Research involving a detainee or a prisoner of war as a human subject is prohibited.

This prohibition does not apply to activities covered by the IND or IDE provisions of the FDA regulations at Title 21, CFR, when the purpose is for diagnosis or treatment of a medical condition in a patient. Such treatment may be offered to detainees or prisoners of war with their informed consent when the medical products are subject to FDA

regulations and only when the same product may be available to DoD-affiliated personnel consistent with established medical practices.

28.12.7.5 DoD-Affiliated Personnel as Subjects

The recruitment and inclusion of DoD-affiliated personnel (i.e., Service members, Reserve Service members, National Guard members, DoD civilians, and DoD contractors) in research must be approached with care and in accordance with the requirements of DoDI 3216.02 and any applicable DoD component requirements. DoD considers DoD-affiliated personnel to be vulnerable to coercion and undue influence due to the nature of the command structure of defense organizations.

Investigators who intend to recruit DoD-affiliated personnel are advised to seek collaboration with a military investigator familiar with DoD and service-specific requirements. A letter of support from Commanders of military facilities or units in which recruitment will occur or the study will be conducted may be required by the Component HRPO and the IRB. Some military sites may also require that personnel seek written permission from their supervisor prior to participation in research.

When the research includes surveys of DoD personnel, investigators are responsible for ensuring that the survey(s) are submitted to and approved by the DoD Information Management Control Officer (IMCO) prior to implementation but after the research is approved by the IRB. When a survey crosses DoD components, investigators are responsible for ensuring that any additional DoD-required reviews and approvals take place before implementing the survey.

Specific requirements of DoDI 3216.02 include the following:

- If the research involves DoD-affiliated personnel as subjects, and the research includes any risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.
- If the research involves DoD-affiliated personnel, the key investigator (the person leading the performance of the research) must receive command or Component approval to execute the research.
- Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research.
- Military and civilian supervisors, officers, and others in the chain of command must not be present at any recruitment sessions or during the consent process for DoD-affiliated personnel. Excluded supervisors or those in the chain of command may participate in separate recruitment sessions, if applicable.
- Service members and all Reserve Component and National Guard members in a federal duty status are considered for purposes of DoDI 3216.02, to be adults. If a Service member, Reserve Component or National Guard member in federal duty

status, student at a Service Academy, or trainee is under 18 years of age, the IRB must carefully consider the recruitment process and the necessity of including such member as a human subject.

- In order to approve research involving DoD-affiliated personnel as human subjects, the IRB or HRPO must determine whether the following requirements have been satisfied:
  - The consent documentation must include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty.
  - For research involving recruitment of DoD-affiliated personnel in greater than minimal risk research, and when recruitment occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:
    - Must not have a conflict of interest with the research or be a part of the research team.
    - Must be present during recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials.
    - Should be available to address DoD-affiliated personnel's concerns about participation.
- Compensation, including non-monetary compensation, to DoD-affiliated personnel for participation in research while on duty is prohibited other than compensation for blood draws (maximum of $50 per blood draw) in accordance with 24 U.S.C. 30. Personnel may be compensated for participation in research when not on duty (e.g., off-hours) in reasonable amounts consistent with local standards and the nature of the research. Plans to compensate subjects must be approved by the IRB.