DEFINITIONS – GLOSSARY OF TERMS

Accounting of Disclosure: The provision for recording a list of disclosures of PHI made by members of Geisinger's covered entities without prior HIPAA authorization.

Administrative Hold: An action initiated by the Investigator in response to an IRB request to place specific research activities on hold temporarily to allow for additional information to be obtained.

Adverse Event: An untoward or undesirable experience or any undesirable experience associated with the use of a medical product in a patient.

Advertising: A public announcement usually by a printed notice or voice or data broadcast that describes a research study including contact information. Typically this is used for recruitment purposes for a research study.

Allegation of non-compliance: An assertion made by a third party that must be proved or supported with evidence.

Anonymous Data: Information that was previously recorded or collected without any of the 18 identifiers as defined by HIPAA, and no code is assigned which would allow data to be traced to an individual.

Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

Authorization: A customized document, usually as a part of the informed consent document, that gives an Investigator permission to use specified protected health information (PHI) for a specific purpose, or to disclose PHI to a third party specified by the Investigator other than for treatment, payment or healthcare operations.

Biostatistical Support: All support provided by the Biostatistics & Research Data Core including, but is not limited to data abstraction from the electronic health record, data manipulation, data management, study design, grant preparations, biostatistical analysis, results presentation and manuscript writing.

Bonus Payment: Compensation tied to the rate or timing of recruitment. Examples of bonus payments include but are not limited to the following: The sponsor announces that the highest enrolling site in the nation will receive a $10,000 bonus; The sponsor offers to pay an additional $10,000 to any site that enrolls five participants within a week; The sponsor offers to pay an additional $10,000 to any site that fulfills its recruitment target

by the end of the month; The sponsor offers to pay an additional $1,000 for any subject who agrees to enroll within one day of initial contact.

Certificate of Confidentiality: A document that provides additional protection of data from legal subpoena. The Certificate provides protection against compelled disclosure of identifying information or other identifying characteristics of a research participant enrolled in biomedical, behavioral, clinical, and other forms of sensitive research.

Children/Minors: According to Federal regulations, 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. In Tennessee, the legal age for consent is 18 years of age.

Clinical Investigation: as defined by FDA 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 studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous... [21 CFR 50.3(c) and 21 CFR 56.102(c)].

Clinical Research: "Human subject research" as defined in 45 CFR 46. A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

Clinical Trial: A prospective biomedical or behavioral research study of human participants involving a licensed or investigational drug, device, biologic, or a behavioral intervention that is designed to answer specific questions about biomedical or behavioral interventions (e.g., treatments, devices, drugs, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe and effective.

Coded Information/Data: For the purposes of this policy, identifying information that would enable the Investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Cognitively Impaired: Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly

diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.

Compassionate Use: The term "compassionate use" is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term "compassionate use" does not, however, appear in FDA or HHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.

Component Analysis: A systematic approach to the ethical analysis of risk and potential benefits in research.

Contact Person – The person responsible for working with the PI to complete the IRB paperwork. This person must either be the main Clinical Research Coordinator (CRC), Project Manager (PM), or responsible resident and/or fellow.

Continuous Quality Improvement (CQI): A methodology employed by the IRB Teams, when needed, to improve existing processes by identifying the root cause of a problem, developing and implementing an action plan, and evaluating the outcome to assure problem resolution. The PDSA cycle incorporates the following process: Plan, Do, Study, Act.

Continuing Non-compliance: A pattern of repeated actions or omissions taken by an investigator or study team member. Such pattern of behavior may indicate a deficiency in the ability or willingness to comply with Federal regulations, State and local regulations, Geisinger Health System policies or the determinations and requirements of the IRB relating to Human Subjects Research.

Coordinating Center: An institution, department, or center, which agrees to be responsible for the conduct, administrative, or coordinating functions of a multi-center research project.

Covered Entity: A health plan, a health care clearinghouse, or a health care provider who transmits health information and is therefore subject to the HIPAA regulations. For the purpose of this policy, any individual creating or accessing Protected Health Information (PHI) for the delivery of healthcare at Geisinger is within the covered entity. RHI (as defined below) is not considered part of the covered entity.

Data Custodian: Any person who develops, maintains, or has access to data with PHI. This includes a researcher with databases from prior research projects, as well as individuals with access to institutional, divisional or departmental databases, including CDIS or the EHR. The Data Custodians have a responsibility to ensure they grant access to data for research purposes to only the PI and their research staff: 1) who have an IRB

approved protocol; or 2) are exempt from review under 45 CFR 46.101; 3) are determined to not be human subjects research; or 4) are requesting access to data under preparatory to research provision.

Data Dictionary: a document that catalogs the organization, contents, and conventions of one or more databases. This typically includes the names and descriptions of various tables and fields in each database, plus additional details, such as the type and length of each data element. There is no universal standard as to the level of detail in such a document. Data dictionaries do not contain any actual data from the database, only bookkeeping information for managing it. Without a data dictionary, however, a database management system cannot access data from the database.

Data and Safety Monitor (DSM): An individual assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have expertise in the relevant medical, ethical, safety and scientific issues.

Data and Safety Monitoring: A plan to oversee the implementation of a study protocol for compliance monitoring.

Data and Safety Monitoring Board (DSMB): A formally appointed independent group consisting of at least three (3) members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include expertise in the relevant field of study, statistics, and research study design.

Data and Safety Monitoring Committee (DSMC): Another term for DSMB.

Data and Safety Monitoring Plan (DSMP): A DSMP describes how the Investigator plans to oversee the research participant's safety and welfare and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study.

Data Sources: A collection of information generated from departmental or system-wide data; medical records (electronic or paper), images, specimens, other information related to the health or care of patients that are in the custody of departments or system-wide, and from prior or other current research projects.

Data Use Agreement (DUA): A satisfactory assurance between the covered entity and a researcher using a limited data set that the data will only be used for specific uses and disclosures.

De-Identified: Health information that meets the standard and implementation specifications for de-identification under § 164.514(a) and (b) and cannot have links for

re-identification. De-identified data is considered not to be individually identifiable health information.

De-Identified Health Information: Health information that has been stripped of all 18 identifiers as defined by HIPAA, so that the information could not be traced back to an individual. De-identified data also pertains to health information that has been assigned and retains a code or other means of identification provided that:

a. The code is not derived from or related to the information about the individual;
b. The code could not be translated to identify the individual; and
c. The covered entity (as described above) does not use or disclose the code for other purposes or disclose the mechanism for re-identification.

Dead Fetus: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

Delivery: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

Deoxyribonucleic Acid (DNA): The chemical inside the nucleus of a cell that carries the genetic instructions for making living organisms.

Designated Record Set shall mean a group of records maintained by or for the Covered Entities that is (i) the medical records and billing records about individuals maintained by or for the Covered Entities; used, in whole or in part, by or for the Covered Entities to make healthcare decisions about individuals. As used herein the term "Record" means any item collection or grouping of information that include Protected Health Information and is maintained, collected, used, or disseminated by or for the Covered Entities.

Deviation: An incident involving noncompliance with the protocol, but one that typically does not have a significant effect on the subject's rights, safety or welfare, and/or on the integrity of the resultant data. Deviations may result from the action of the participant, Investigator, or staff. *NOTE: This definition may not match the PI or Sponsor's definition.*

Disclosure: The release, transfer, access to, or divulging of information in any other manner outside the covered entity holding the information.

Directed Audit: These audits are conducted by the Office of Research Compliance (ORC) to assess the Investigator's compliance with federal regulations, state and local laws, and Geisinger IRB policies and procedures. These audits of IRB approved research studies are in response to identified concern(s). Concerns may be identified by an IRB Committee, an external source (e.g. OHRP, FDA or Sponsor), or an internal source (e.g. participant, family member, or Institutional personnel).

Disclosure of PHI: The release, transfer, or provision of access to, or divulging in any manner of information outside of the covered entity.

Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

Electronic Media shall mean the mode of electronic transmissions. It includes the Internet, extranet (using Internet technology to link a business with information only accessible to collaborating parties), leased lines, dial-up lines, private networks, and those transmissions that are physically moved from one location to another using magnetic tape, disk, or compact disk media.

Eligible Projects: To receive funding from the Geisinger Research Board Designated Endowment Fund, research projects must be initiated by Geisinger investigators and based at Geisinger. Projects initiated by non-Geisinger investigators are not eligible for support. Applications for funding must include at least one member of the clinical staff as the principal or collaborating investigator.

Emergency Response: A public health activity undertaken in an urgent or emergency situation, usually because of an identified or suspected imminent health threat to the population, but sometimes because the public and/or government authorities perceive an imminent threat that demands immediate action. The primary purpose of the activity is to document the existence and magnitude of a public health problem in the community and to implement appropriate measures to address the problem (Langmuir, 1980).

Emergency Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

Emergency Treatment IND: A mechanism through the FDA for providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

Emergency Use: The use of an investigational drug, agent, biologic, or device with a human subject in an immediate serious life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

Enrollment Incentives (Bonuses): A financial contribution as a reward to investigators based on being faster-enrolling study site. Examples include:

- investigators or research staff are contacted by the sponsor or contract research organization (CRO), urging them to meet enrollment goals and offer additional payments for each subject.
- the sponsor offers to pay the investigator his/her research staff for accelerated enrollment, such as, an additional $1,000 if they are the first site to enroll 20 subjects.

Evaluation: The systematic application of scientific and statistical procedures for measuring program conceptualization, design, implementation, and utility; making comparisons based on these measurements; and the use of the resulting information to optimize program outcomes (Rossi and Freeman, 1993; Fink, 1993).

Expired Study: When continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. The study expires on the date specified on the approval letter and the informed consent document. No activities can occur after the expiration date.

Fetus: The product of conception from implantation until delivery.

Finder's (Referral) Fees: Contribution of value or perceived value (of any type; e.g. cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) to an individual made in exchange for referral or recruitment of a participant to a research study. This would include payments to a resident, physician, nurse, or other in a position to identify potential participants that might qualify for enrollment into a study). Examples include:

- the investigator agrees to give the local primary care physicians and their staff $1,000 for every patient that referred for enrollment in the trial.
- the investigator agrees to provide local primary care physicians and their staff gift certificates for each patient that is referred for enrollment in the trial.

Finding of Non-Compliance: A proven or obvious incident of non-compliance.

Food and Drug Administration (FDA): The FDA is the federal oversight agency responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

Good Clinical Practice (GCP): International ethical and scientific quality standard for designing, conducting, monitoring, recording, auditing, analyzing and reporting studies. Insures that the data reported is credible and accurate and that subject's rights and confidentiality are provided.

Greater than Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Group C Treatment Investigational New Drug (IND): A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually

have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the Geisinger IRB requires prospective IRB review and approval.

HMORN – research conducted in more than one member of the HMO Research Network (HMORN). Data-only studies in epidemiology, health services, health economics, and related research areas.

Health Care Decision-Maker: In the case of an incompetent individual, or a individual who lacks decision-making capacity, the individual's health care decision-maker is designated in order of preference as one of the following: the individual's court-appointed legal guardian or conservator with health care decision-making authority (e.g., Durable Power of Attorney for Health Care or DPAHC); the individual's health care agent as specified in an advance directive; or the individual's Health Care Decision-Maker.

Health Care Operations shall have the meaning set forth in 45CFR164.501.

Human Fetal Tissue: Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.

Human Immunodeficiency Virus (HIV): Any of the lentiviruses and especially HIV-1 that infect and destroy helper T-cells of the immune system causing the marked reduction in their numbers that is diagnostic of AIDS.

Human Research Protection Program (HRPP): The HRPP exists to promote high quality, ethical research. HRPP does this by serving as the advocate for the rights and welfare of persons who participate in research programs conducted by Geisinger Health System faculty, staff, students, and researchers. The HRPP has responsibility for review of research involving human subjects conducted within the Geisinger Health System. The HRPP assists researchers in complying with federal, state and Geisinger Health System policies regarding experimentation involving human subjects, and oversees the review and conduct of research conducted by federally registered *Institutional Review Boards* (IRBs).

Human subject: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

Human Subjects Research Study: A research study involving human subjects that is conducted or sponsored by Geisinger.

Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.

Humanitarian Use Device Exemption (HDE): A Federal Drug Administration (FDA) approval for a physician to use a HUD in clinical treatment or as the subject of a clinical investigation.

IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution. A Memorandum of Understanding is required designating the relationship.

Incentive: Financial payments and/or other inducements to investigators, research staff, or referring physicians to promote enrollment of subjects in research study. These do not include payments to subjects themselves. Examples include:

- the sponsor provides financial reimbursement to the research and/or study staff that exceeds the fair market value of the services provided.
- the sponsor provides payment or services outside the scope of the research study requirement, such as, unrestricted educational grants.

Individually Identifiable Health Information shall mean information that is a subset of health information, including demographic information collected from an individual, and is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (ii) related to past, present or future physical or mental health or condition of an individual; the provisions of health care to an individual; or the past, present or future payment for the provisions of health care to an individual; and (a) identifies the individual, or (b) with respect to which there is a reasonable basis to believe the information can be use to identify the individual.

Immediate Family Member: Spouse, domestic partner, or child.

Independent Ethics Committee (IEC): A specially constituted review body whose responsibility is to ensure the protection of the rights, welfare and safety of research participants. An IEC shares the same composition and operations as an Institutional Review Board.

Individual Conflict of Interest: A circumstance such that any action or decision in which an individual is substantially involved with the research may have direct or predictable effect on a financial interest of the individual, spouse, minor child, or organization in which the individual serves as an officer, trustee, partner or employee.

Individually Identifiable Health Information: Any information collected from an individual (including demographics) that is created or received by a health care provider, health plan, employer, and/or health care clearinghouse that relates to the past, present or future physical or mental health or condition of an individual, or the provision of health care to an individual or the past, present or future payment for the provision of health care to an individual and identifies the individual and/or to which there is reasonable basis to believe that the information can be used to identify the individual.

Institutional Official: The individual identified on the Federalwide Assurance with OHRP as authorized leader of the Hospital's human subject protection program.

Institutional Review Board (IRB): A specially constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in biomedical or behavioral/social science research.

Interaction: Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.

Intervention: Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the participants' environment that are performed for research purposes.

Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.

Investigational Device: Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.

Investigational Device Exemption: A FDA approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.

Investigational Drugs/Investigational Biologics (Test Articles): A new drug or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used *in vitro* for diagnostic purposes. Investigational drugs or biologics may include:

a. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or
b. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).

Investigational New Drug (IND): FDA granting of permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data that has determined that a particular product is safe and effective for a specific use. The FDA

permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

Investigator-Sponsor; Individual with both responsibilities of initiating and conducting a clinical trial.

Key Research Personnel: The Principal Investigator and any professional research staff member, whether employed by, or otherwise affiliated with, Geisinger, involved in exercising independent judgment in research design, enrollment, data collection and gathering, data analysis and/or preparation for publication.

Legally Authorized Representative: An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities.

Limited Data Set: A set of data (protected health information) that may be used for research, public health or health care operations without an authorization or waiver of authorization, which excludes direct identifiers of the individual or of relatives, employers, or household members of the individual, with the exception of city, state, ZIP Code, elements of dates, and other numbers, characteristics, or codes not listed as direct identifiers.

Local Research Context: Knowledge of the institution and community environment in which human research will be conducted.

Memorandum of Understanding (MOU): A formal agreement between Geisinger and another institution that identifies the Geisinger Institutional Review Board as the IRB of record for that institution.

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. [45 CFR 46.102(i)][21 CFR 56102(i)].

Minimum Necessary Standard: The least information reasonably necessary to accomplish the intended purpose of the use, disclosure, or request of PHI.

Minor Non-Compliance: means any non-compliance that is not serious or continuing noncompliance. For example, minor noncompliance might include the following violations: (1) missing an original signed and dated research consent form; (2) missing pages of executed research consent forms; (3) inappropriate documentation of informed consent, e.g., missing one or more signatures or date; (4) obtaining informed consent using an invalid/outdated research consent form that contains all of the information required by the IRB; (5) failure to submit continuing review forms/documents prior to expiration of IRB approval; (6) unplanned deviation from the approved protocol where

the deviation does not impact the rights and welfare of subjects or the integrity of the research.

Monitor: Person employed by the sponsor or CRO who reviews study records to determine that a study is being conducted in accordance with the protocol. A monitor's duties may include, but are not limited to, helping to plan and initiate a study, and assessing the conduct of studies. Monitors work with the clinical research coordinator to check all data and documentation from the study.

Monitoring: Reviewing a clinical study, ensuring conduct, proper records and reports are performed as stated in the clinical protocol, standard operating procedures, GCP and by regulatory requirements.

Neonate: A newborn.

Non-Clinical Research: Research that does not involve living human beings, for example bench research.

Non-compliance: Failure to comply with applicable Federal regulations, state and local regulations, Geisinger Health System policies or the determinations and requirements of the Geisinger Health System relating to human subjects research.

Non-Human Subjects Research: Any activity determined by the IRB to not represent "Human Subjects Research."

Non-significant Risk (NSR) Device Study: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants.

Nonviable Neonate: A neonate after delivery that, although living, is not viable.

Office for Human Research Protections (OHRP): The office under the Department of Health and Human Services (DHHS) responsible for implementing the DHHS regulations (45 CFR 46) governing biomedical and social/behavioral sciences research involving human participants.

Open – Label Protocol: A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.

Parallel Track: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that "parallel" the controlled clinical trials and are essential to establish the

safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the Geisinger IRB.

Participant Advocate or Advocacy Group: An individual or group of individuals that seek to safeguard the rights and welfare of research participants.

Performance Site(s) Engaged in Research: A performance site becomes "engaged" in human subjects research when its employees or agents 1) intervene or interact with living individuals for research purposes, or 2) obtain individually identifiable private information for research purposes. Further, a performance site is considered to be "engaged" in human subjects research when it receives a direct Federal award to support the research.

Periodic Compliance Review: Random assessments of the internal IRB department and external departments or sites involved in the conduct of human subjects research at Geisinger conducted by the IRB Process Improvement Team. These reviews are used to evaluate proper execution and accurate documentation of an IRB approved research project. Internal compliance reviews monitor the adherence to federal regulations, state and local law, and IRB policies and procedures as well as accurate documentation between the IRB database and the IRB paper files. External compliance reviews monitor the adherence to federal regulations, state and local law, Geisinger IRB policies and procedures, adherence to the study protocol, accurate documentation and reporting of study related activities, and evaluation/observation of the informed consent process.

Pregnancy: Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.

Preparatory to Research: Any action taken in assessing the research question or hypothesis, such as accessing medical records, querying of databases for any type of individually identifiable health information, or any activity where PHI is accessed to prepare a research protocol.

Principal Investigator - Geisinger-employed permanent professional staff with advanced degrees (MD, DO, or PhD) by virtue of their appointment at Geisinger. Members of the nursing staff may serve as PI upon approval of the Nursing Research Council. Temporary professional staff may serve as PI on non-therapeutic/minimal risk studies. Temporary staff may only serve as PI on a study with therapeutic intent or more than minimal risk if a member of the permanent professional staff serves as a Sub-Investigator. Health system staff, such as respiratory therapists, perfusionists, etc. may not serve as PI. Resident, fellows, and other trainees may not serve as PI.

Privacy Board: A review board that is responsible for approving HIPAA waivers of authorization. At Geisinger the Geisinger IRB's serve as the privacy board.

Privacy Standards shall mean the Standards for Privacy of Individually Identifiable health Information, 45CFR parts 160 and 164.

Private Information: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.

Program Evaluation: An essential organizational practice in public health using a systematic approach to improve and account for public health actions (Centers for Disease Control and Prevention, 1999)

Prospective: Research utilizing human participants' specimens/data that will be collected after the research is approved by the IRB.

Protected Health Information (PHI): Any information, whether oral or recorded in any form or medium, that is created or received by a health care provider and relates to the past, present or future physical or mental health or condition of an individual.

Protocol: Documentation of study objective, design, methods, statistical methods and organization. The term also includes amendments made to the original document.

Psychotherapy Notes: 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 that are separated from the rest of the individual's medical record. Psychotherapy notes exclude 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.

Quality Assurance Reviews: Quality Assurance reviews are performed by the IRB Teams to verify that the electronic database is consistent with the IRB paper files and the paper files are collated in accordance with IRB policy and procedure

Quality Assurance/Quality Improvement –

Prisoners: any individual involuntarily confined or detained in a penal institution encompassing:

- individuals sentenced to such an institution under a criminal or civil statute
- individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution
- individuals detained pending arraignment, trial, or sentencing

Re-identification means using a code or other means of record identification to allow information that was de-identified to be re-identified.

Recruitment: Seeking individuals to enroll or participate in a research project.

Reimbursement; See research payment.

Related: An event is "related" if it is likely to have been caused by the research procedures.

Repository: A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple Investigators or multiple research projects.

Research: Any systematic investigation (including research development, testing and evaluation) designed to develop or contribute to generalizable knowledge.

Researcher: The Principal Investigator and is someone who is professionally engaged in research. He/she must be Geisinger-employed permanent professional staff with advanced degrees (MD, DO, or PhD) by virtue of their appointment at Geisinger.

Research Audit: An independent assessment and evaluation of an institution's activities. To meet the highest standards, audits are performed in accordance with established standards.

Research Health Information (RHI): Individually identifiable health information that is or has been collected solely for the purposes of research.

Research Misconduct: Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or differences of opinion.

Research Payments: Cash and non-cash payments for reimbursement of time and expenses associated with participation in research activities.

Research Team: Investigator, sub-investigator and clinical research coordinator involved with the study.

Resident/Fellow: Research conducted by residents and/or fellows must be under the direction of a PI staff mentor. The principal investigator may delegate the performance of

any or all components of the research to non faculty if allowed under the Pennsylvania state law and certify to the IRB that the individuals are sufficiently trained to performed the functions assigned.

Retrospective: Research utilizing human participants' specimens/data that were previously collected (e.g., on the shelf) before the research was submitted to the IRB.

Scientific Misconduct: Means any fabrication, falsification, plagiarism, or other practice that seriously deviates from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research.

Sensitive Information: Includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information, that if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information.

Serious: An event is "serious" if it involved a serious harm to one or more persons (who may or may not be participants), or required intervention to prevent one or more persons from experiencing serious harm.

Serious non-compliance: An action or omission taken by an investigator or study personnel that: 1) may adversely affect the rights and welfare of human subjects; **or** 2) may compromise the integrity of the research.

Significant Financial Interest: Any of the following financial interests of any key research personnel, or his or her immediate family, in aggregate. (The thresholds described below apply to the aggregate ownership of a key research personnel and his or her immediate family. For example, if an Investigator, his/her spouse, domestic partner and dependent children own together $10,000 or 5% worth of equities in the sponsor). The thresholds do not apply to the combined ownership of all Investigators:

a. Compensation whose value could be affected by the study outcome.
b. A proprietary interest in the tested product included but not limited to, a patent, trademark, copyright or licensing agreement, or the right to receive royalties from product commercialization.
c. Any equity interest in the sponsor or product whose value cannot be readily determined through preference to public prices (e.g., ownership interest or stock options).
d. Any equity interest in the sponsor or product that exceeds $10,000 or 5% ownership interest.
e. Significant payments or other sorts with a cumulative value of $10,000 made directly by the sponsor as an unrestricted research or educational grant, equipment, consultation, or honoraria, or other payment.

Significant Risk (SR) Device Study: A study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Sponsor-Imposed Suspension: A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; response to a DSMB report/recommendation; or a preplanned stopping point.

Sub-investigator: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows).

Subject: as defined by FDA means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or have a medical condition or disease [21 CFR 812.3(p)].

Surveillance: The ongoing, systematic collection, analysis, and interpretation of outcome-specific data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease or injury (Thacker and Berkelman, 1988).

Suspension of Approval of Research/Suspend Approval: An action taken by the IRB for any reason to temporarily or permanently withdraw approval for some or all research activities short of permanently withdrawing approval for all research activities.

Test Article: as defined by FDA 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).

Termination of Previously Approved Research/Terminate: An action taken by the IRB for any reason to permanently withdraw approval for all research activities (except for those follow up procedures which are necessary to protect the health or welfare of the subjects).

Therapeutic Intent: Drugs, surgical procedures, and behavioral interventions that are administered on the basis of evidence sufficient to justify the believe that they may benefit subjects.

Third-party: Any person or vendor (external to the University) who receives payment for providing research-related services and/or products.

Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.

Treatment IND or Biologics: A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Prospective IRB review and approval is required.

Unanticipated: An event is "unanticipated" when it was unforeseeable at the time its occurrence. The word unanticipated, is not a synonym for unexpected. A research protocol can monitor for an unexpected event, but cannot monitor for an unforeseen event. All unanticipated events are unexpected, but not vice versa.

Unanticipated Adverse Device Effect: 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 to participants or others associated with a device that relates to the rights, safety, or welfare of participants.

Unanticipated Problems Involving Risk to Participants or Others: Any event that was (1) unanticipated, (2) serious, and (3) related.

Unexpected: An event is "unexpected" when its specificity, nature, severity or incidence are not accurately reflected in the information previously reviewed and approved by the IRB.

Unlimited Data Set: is a set of identifiable patient data that may be used for research, public health or health care operations with waiver of authorization and tracking of disclosures.

Use means, with respect to individually identifiable health information, the sharing, employment, application, utilization, examination, or analysis of such information within an entity holding the information.

Use of PHI: Querying, viewing, and/or extracting any protected health information for research purposes within the covered entity.

Whistle-blower: An individual who reports sensitive information to the Geisinger IRB regarding potential non-compliance issues or research activities that have potentially placed participants or others at increased risk in relationship to the conduct of the research.

Work scope: Initial assessment of projected number of Biostatistical support hours required for completion of the study.

Viable: As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Violation: Accidental or unintentional changes to or not compliant with the IRB approved protocol that affect the subject's rights, safety, welfare, and/or the integrity of the resultant data. *NOTE: This definition may not match the PI or Sponsor's definition.*