Glossary

510(k) clearance - A 510(k) clearance or premarket notification [(510(k)] submission is a route the FDA uses to approve a medical device. If the FDA agrees the new device is substantially equivalent to a legally marketed device for which a premarket approval (PMA) is not required, the manufacturer may market it immediately.

AAHRPP: Association for the Accreditation of Human Research Protections Programs, Inc., is an independent, non-profit accrediting body that ensures that human research protections programs (HRPPs) meet established standards for research quality and human subjects protections.

Adverse Event: Any untoward physical or psychological occurrence in a human subject participating in research. It can be any unfavorable and unintended event, including an abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article. It does not necessarily have to have a causal relationship with the research.

Adverse Drug Reaction (ADR); when identified before market approval means any noxious and unintended response to a medicinal product related to any dose; causal relationship between the medicinal product and an ADR is at least a reasonable possibility. ADRs identified after market approval defined as any noxious and unintended response to a drug that occurs at doses normally used in individuals to prevent, diagnose, or treat disease or to modify physiological function (ICH 2016).

Amendment: Any change made by correction, addition, or deletion to the previously approved research proposal. Minor Change: A minor change is one which, in the judgment of the PHCIRB Designated Reviewer, makes no substantial alteration in (i) the level of risks to subjects; (ii) the research design or methodology (e.g., an addition of a procedure which would increase risk to subjects); (iii) the number of subjects enrolled in the research (increasing the approved number of subjects by greater than 20% of the currently approved number of subjects); (iv) the qualifications of the research team; or (v) the facilities available to support safe conduct of the research.

A minor change does NOT include the addition of any procedure that involves more than minimal risk or does not fall into categories (1)-(7) of research that can be reviewed using expedited review.

Anticipated (expected) Adverse Event: An adverse event that is not an unanticipated adverse event. It is expected and should be stated in the consent form document, protocol, and investigator's brochure, as applicable.

Approval Pending: The status of a research protocol that has been submitted and reviewed by the IRB and is missing minor supporting documentation or simple changes necessary for approval. The PI may not begin any activities under the research protocol until the IRB Chair, Vice Chair or a designated reviewer accepts the information/changes on behalf of the Piedmont Healthcare IRB. This determination specifies conditions under which research can be approved, pending the completion of minor clarifications or modifications to the protocol, informed consent document(s) and/or accompanying document(s). The IRB may designate the IRB Chairperson (and/or other individual(s) with appropriate expertise or qualifications) to review responsive materials from the investigator and determine that the conditions have been satisfied, and further review by the IRB at a subsequent convened meeting would not be necessary. The proposed research may not begin until a letter of approval is received from the IRB.

Approved: The determination by the IRB that the research protocol and supplemental information have been reviewed and meet all criteria for approval. Determination given when all criteria for approval are met to satisfaction in accordance with 45 CFR 46.111 as well as institutional, federal, state and local.

Audit: A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements.

Authorization Agreement: Document that notes the ceding of PHCIRB oversight to a particular IRB and outlines the responsibilities of both parties related to initial and continuing review of a research study.

Belmont Report: A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978. Ethical principles that define 'respect for persons', 'beneficence', and 'justice' as they relate to human subjects in research.

Beneficence: The ethical concept that states that welfare of research participants should be a goal of a research study.

Bioavailability: The degree to which, or the rate at which, a medication or other substance is absorbed or becomes available at the targeted place in the body.

Biological Product (or Biologic): Any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries.

Business Associates: Persons or entities that create, use, or disclose PHI to perform or assist in the functions of a covered entity.

Case Report Form (CRF): The tool that is used to record data collected during a clinical trial. The CRF is submitted to the sponsor.

Central IRB: For multisite studies, this is the regulatory body designated to conduct reviews of the research on behalf of all participating sites agreeing to a centralized review process. Piedmont Healthcare will agree to rely on the reviews of central IRBs that have obtained full AAHRPP accreditation.

Certificate of Confidentiality: A certification granted by NIH to protect identifiable study data from forced or compelled disclosure. Regardless of funding source, NIH may grant a Certificate of Confidentiality to protect information that: (1) is identifiable; (2) is for research approved by the IRB; and (3) constitutes sensitive information.

Clinical Trial (also referred to as a clinical investigation or study): Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), whether approved for marketing or not, and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its efficacy and/or safety.

Clinical Trial: A biomedical or behavioral research study of human subjects designed to answer specific questions about diagnostic procedures or therapeutic interventions (drugs, treatments, devices, or new ways of using known drugs, treatments or devices). Clinical trials are used to determine whether new diagnostic procedures or therapeutic interventions are safe, efficacious, and effective.

Coded Information: Information that would enable the investigator to readily ascertain the identity of the individual or individual specimen that has been replaced with a number, letter, symbol, or combination thereof. A key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Common Rule: The federal policy for the protection of human subjects.

Compassionate Use (Expanded Access): FDA authorized use of an investigational drug (or biologic product) to treat patients with serious or life-threatening diseases or conditions who have no satisfactory or comparable alternative therapy to diagnose, monitor, or treat the disease or condition.

Conflict of Interest (IRB Member): Any situation in which financial or personal obligations may compromise or present the appearance of compromising an individual or group's professional judgment in conducting, reviewing, or reporting research. This may also include spouse's, domestic partner's, or dependent children's financial interest.

Consent Form (also called Informed Consent Document): The document that includes the information needed for potential subjects to have sufficient information to provide informed consent to participate in a clinical trial.

Continuing non-compliance: A pattern of repeated non-compliance that indicates a lack of ability or willingness to adhere to policies or regulations; or repeated noncompliance that if allowed to continue is likely to increase risk, adversely affect the rights, welfare and safety of research participants, or adversely affect the scientific integrity of the study.

Continuing Review: IRB reassessment of previously reviewed and approved research based on the gathered information on the conduct of the study.

Controlled: Controlled means that subjects are split into at least two groups: those receiving the experimental agent and those receiving a standard treatment for the condition (an active control), no treatment, or a placebo. If subjects are assigned randomly into these groups, the study is a randomized controlled trial.

Corrective Action Plan (CAP): A plan developed by an investigator, with or without the assistance and guidance of the IRB, following root cause analysis into an instance of noncompliance or other problems in the conduct of human subjects research. The CAP must include measures designed to correct the immediate problem and prevent its recurrence. CAPs are reviewed and maybe modified by the IRB before being approved.

Covered Entity: Health care providers, health plans, and health care clearinghouses that must comply with requirements to protect the privacy and security of health information and provide individuals with rights with respect to their health information.

Data and Safety Monitoring Board (DSMB): A formally appointed independent group consisting of physicians, statisticians, and others assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of human subjects, relevance of the study question, appropriateness of the study, and integrity of the accumulating data.

Data Safety Monitoring Plan (DSMP): An individualized plan, written by the Principal Investigator responsible for the study. The DSMP will oversee the Human Subject'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.

Deferral: The decision by the IRB to postpone approval and table further discussion concerning a protocol until certain information/instruments are submitted for review.

Designated Reviewer: An experienced IRB member designated to perform an expedited review, preferably in writing. To be eligible for consideration as a Designated Reviewer, the person must be a PHCIRB member who meets current training requirements. A member of the PHCIRB who

has been designated to perform expedited reviews, preferably in writing. To be eligible for consideration as a Designated Reviewer, the person must be a PHCIRB member who meets current training requirements.

Department of Health and Human Services (HHS): The United States government's principal agency for protecting the health of all Americans and providing essential human services.

Device: A constructed tool 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.

Disapproval/Disapprove: The determination by the IRB that a reviewed submission lacks information necessary to meet with approval criteria. Determination given if the proposed research fails to meet one or more criteria outlined in the regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D. The IRB will send a detailed letter to the research outlining all reasons of disapproval. The investigator will have an opportunity to respond in person or in writing.

Drug Supplier/Manufacturer means: in addition to producing the drug, the company also supplies the investigator with the drug for use in the study.

Emergency Research: A planned clinical investigation that requires prior written FDA authorization to proceed. The investigation will involve subjects who are in a life-threatening situation for which available treatments are unproven or unsatisfactory.

Emergency use: the use of a test article on 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. [21 CFR 56.102(d)]

Engaged in Research: An institution is considered to be engaged in research whenever its employees or agents for the purpose of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them, or (2) identifiable private information about the subjects of the research.

Enrolled: When a subject gives informed consent to participate, he or she is considered to be enrolled in a study.

Essential Documents: are defined by ICH (2016) E6 Section 1.23 as the documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

Exempt Research: A classification of projects that do not require IRB continuing review and are not subject to requirements under 45 CFR 46. Studies that may qualify for exempt review must still be submitted to the IRB for review.

Expanded Access: FDA authorized use of an investigational drug (or biologic product) to treat patients with serious or life-threatening diseases or conditions who have no satisfactory or comparable alternative therapy to diagnose, monitor, or treat the disease or condition.

Expedited Review: A level of IRB review that does not require the expertise of the full committee. To qualify for this review level a proposal must involve no more than minimal risk and/or minor changes in approved research.

Expiration Date: The date on which protocol approval expires. If the request for continuing approval of the protocol is not submitted prior to the expiration date, all research related activities shall stop except for limited subjects safety measures.

FDA Regulations: The rules set forth by the U.S. Department of Health and Human Services, Food and Drug Administration through Title 21 of the Code of Federal Regulations.

Federalwide Assurance (FWA): An assurance of compliance is a written document submitted by an institution that is engaged in non-exempt human subjects research conducted or supported by HHS. Through the assurance, an institution commits to HHS that it will comply with the requirements set forth in the regulations for the protection of human Subjects per 45 CFR 46.

The assurance of compliance with applicable federal regulations for the protection of Human Subjects in all Research conducted under the auspices of the institution holding the assurance and that is conducted or supported by any U.S. department or agency that has adopted the Common Rule. An FWA is approved by OHRP, as an agency of DHHS, for federal-wide use, and therefore, other federal departments and agencies that have adopted the Common Rule may rely upon the FWA for the Human Subjects Research that they conduct or support.

Final Approval Date: When a Research protocol is granted Approval Pending, the PI must provide the IRB Committee with documentation that he/she has provided any additional information or made any changes requested by the IRB Committee. The PI may not begin any activities under the Research protocol until the IRB Chair, Vice Chair or a designated reviewer accepts the information/changes on behalf of the Piedmont Healthcare IRB. The date on which the information/changes are accepted is the Final Approval Date, and the Piedmont Healthcare IRB shall send a written notice that sets forth the Final Approval Date and notifies the PI that the Research protocol is now approved.

Food and Drug Administration (FDA): A federal agency of the United States Department of Health and Human Services. The FDA is responsible for ensuring that the drugs and medical devices marketed in the United States are safe and have a greater benefit than risk when used according to manufacturer's directions.

Full Committee: A majority of the membership of the IRB, including at least one member whose primary concerns are in a nonscientific area.

Generalizable Knowledge: Knowledge from which general conclusions will be drawn. A study that is designed to develop or contribute to Generalizable Knowledge is one that is designed and intended to draw conclusions, inform policy or generate generalizable findings.

Good Clinical Practice (GCP): is a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials.

Greater than minimal risk: Places participants at higher risk than those ordinarily met in daily life or during the performance of routine physical care.

HDE holder: the individual who obtains the Humanitarian Device Exemption (HDE) from the FDA.

Health Insurance Portability and Accountability Act (HIPAA): HIPAA is the Health Insurance Portability and Accountability Act, the federal law passed in 1996 that provides national standards and privacy protections for health information.

HHS Regulations: The HHS Regulations set forth the Federal Policy for the Protection of Human Subjects.

HHS Regulations' Definition of Human Subject: A living individual about whom an investigator (whether professional or student) conducting Research obtains: (a) data through intervention or interaction with the individual; or (b) Identifiable Private Information.

High Risk: Research with no direct benefit to the research subject but which has benefit for research-in-general and for the benefit of future possible "groups" or "classes" of persons with the same or similar diseases or conditions, and for the advancement of scientific knowledge, or for obtaining information which could not be obtained in any other way.

HIPAA Authorization: It is an individual's signed permission to allow a covered entity to use or disclose the individual's protected health information (PHI) that is described in the Authorization for the purpose(s) and to the recipient(s) stated in the Authorization.

HIPAA Identifiers:

- Name
- Address (all geographic subdivisions smaller than state, including street address, city county, and zip code)
- All elements (except years) of dates related to an individual (including birthdate, admission date, discharge date, date of death, and exact age if over 89)
- Telephone numbers
- Fax number
- Email address
- Social Security Number
- Medical record number
- Health plan beneficiary number
- Account number

- Certificate or licence number
- Any vehicle or other device serial number
- Web URL
- Internet Protocol (IP) Address
- Finger or voice print
- Photographic image - Photographic images are not limited to images of the face.
- Any other characteristic that could uniquely identify the individual

HIPAA Privacy Rule: It establishes national standards to protect individuals' medical records and personal health information. Signed permission from individuals is generally required before a covered entity can use or disclose the individual's PHI for research purposes.

HIPAA Waiver/Waivers of HIPAA Authorization: Piedmont Healthcare IRB may grant a complete or partial waiver of the HIPAA Authorization requirement and permit a researcher working in or receiving information from a Piedmont Healthcare entity to access identifiable health information without a subject's written HIPAA Authorization.

Human Subject: A living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information, per DHHS 45 CFR 46.102(f). FDA regulations define human subject as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

Human Subjects Research: Any research or clinical investigation that involves Human Subjects.

Human Subject (FDA Definition): An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a health individual or a patient.

Human Subject (HHS Definition): A living individual about whom an investigator (whether professional or student) conducting research obtains (1) information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens, or (2) obtains, uses studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Humanitarian Use Device (HUD): A medical device intended to benefit patients in the treatment and diagnosis of disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

Humanitarian Use Device Exemption: A premarket approval application submitted to the FDA Seeking a Humanitarian Device Exemption from the safety and effectiveness requirements of sections 514 and 515 of the food, drug, and cosmetic act. The HDE allows a physician to use an HUD in clinical treatment or in clinical investigation. An approved HDE authorizes marketing of an HUD.

Identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. **NOTE:** If it isn't identifiable, it doesn't involve human subjects, and is not under the Common Rule.

Identifiable private information is private information for which the identify of the subject is or may readily be ascertained by the investigator or associated with the information. **NOTE:** If it isn't identifiable, it doesn't involve human subjects, and is not under the Common Rule.

Impartial Witness: a person, who is independent of the trial, who cannot be unfairly influenced by people involved in the trial, who attends the informed consent process if the subject or the subject's legally authorized representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Independent Piedmont Affiliated Physicians: physicians who are not employed by Piedmont Healthcare.

Individually Identifiable Health Information: Includes demographic information that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Individually Identifiable Private Information: A subset of health information, including demographic information collected form an individual, and that (a) is created by or received from a health care provider, health plan, employer, or health care clearinghouse and (b) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to individual; or the past, present, or future payment for the provision of health care to an individual; and 1. That identifies the individual; or 2. With respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Individually Identifiable: Information in a form such that the identity of the Human Subject is or may readily be ascertained by the investigator or associated with the information.

Informed Consent: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research. Individuals capable of giving informed consent should be of sound mind, mentally unimpaired, conscious, and physically able to read and/or hear and understand the elements of informed consent. In addition, they must not have been declared to be legally incompetent.

Inspection: an act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

Institutional Official (IO): The IO is the hospital official responsible for ensuring that the Piedmont Human Research Protections Program has sufficient resources and support needed to comply with federal regulations and guidelines that govern human subjects research. This individual is authorized to represent the hospital and is the signatory official for all assurances. The individual authorized to act for the institution and assume overall responsibility for compliance with the federal regulations, provide sufficient resources for Piedmont Human Research Protections Program, and to ensure the integrity and functionality of institution's program for the protection of human subjects.

Institutional Review Board: A convened group formally designated by an institution to review, approve the initiation of, and to conduct period review of, biomedical and social behavioral research involving human subjects.

Interaction: Includes communication or interpersonal contact between investigator and subject.

Intervention includes physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Investigational agent: A substance that has been tested in the laboratory and has been approved by the U.S. food and Drug Administration (FDA) for testing in People. Clinical trials test how well investigational agents work and whether they are safe to use. This includes agents that may be approved by the FDA for use in one disease or condition but still be considered investigational in other diseases or conditions.

Investigational device: It is a medical device that is the object of a clinical study designed to evaluate the effectiveness and/or the safety of the device. This includes devices that may be approved by the FDA for use in one condition or disease but still be considered investigational in other conditions or diseases.

Investigational device exemption (IDE): Allows the investigation device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification submission to Food and Drug Administration.

Investigational new drug (IND): A drug that has not been approved for general use by the Food and Drug Administration but is under investigation in clinical trials regarding its safety and efficacy.

Investigator: An individual (whether professional or student) who conducts research and under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

Investigator's Brochure: is a compilation of the clinical and nonclinical data on the investigational product and serves as a resource for investigators, institutional review boards/independent ethics committees (IRBs/IECs) during the conduct of a clinical trial.

IRBNet: Secure web-based protocol tracking system adopted by the Piedmont entity.

Key personnel: Individuals with significant roles in assisting the principal investigator in carrying out the research. These persons will have contact with participants and/or their research data and identifiers for purposes of conducting a research study. This includes principal investigators, co-investigators, sub-investigators, research coordinators, and any other research team members who have contact with research participants and/or participants' research data and identifiers. Individuals whose primary contact with the participants is in the context of clinical care, but offer no additional role in research, are not considered key research personnel.

Legally Authorized Representative: 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. Such designation is necessary for cases of medical incapacitation and diminished competence.

Life-threatening: means disease 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 subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Limited Data Set: A limited set of identifiable patient information as defined in the Privacy Regulations issued under the Health Insurance Portability and Accountability Act (HIPAA).

Minimal Risk: 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.

Minimal Risk for Prisoners: The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. The definition for this population identifies a "Healthy person" as the comparison group against which the risks of the research should be measured.

Minimum Necessary Rule: In determining the type and scope of the PHI for which the PHCIRB determines use or access under a waiver or alteration of the HIPAA Authorization requirement is necessary, the IRB must limit access to only that PHI which is reasonably necessary to accomplish the purpose for which the request is made.

Monitor: an individual designated by a sponsor or contract research organization to oversee the progress of an investigation.

Monitoring: the act of overseeing the progress of a clinical trial, and of ensuring it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s). Monitoring is a research sponsor's obligation under GCP and regulations (refer to the module, Monitoring Clinical Trials by Industry Sponsors). Monitoring may be on-site, centralized (also known as remote), or a combination of both.

Neonate of uncertain viability: one where it is not yet determined whether it is capable of surviving to the point of independently maintaining heartbeat and respiration.

Non Affiliated Member: An IRB member who is not associated with Piedmont Healthcare.

Non Compliance: Failure to act in accordance with institutional policies and/or regulations, governing human participant research, and/or the requirements or determination of the PHCIRB.

Continuing non-compliance: a pattern of repeated non-compliance that indicates a lack of ability or willingness to adhere to policies or regulations; or repeated non-compliance that if allowed to continue is likely to increase risk, adversely affect the rights, welfare and safety of research participants, adversely affect the scientific integrity of the study.

Serious non-compliance: failure to act or willful violation of policies or regulations which create increased risks to research participants, adversely affects the rights, welfare and safety of research participants or adversely affects the scientific integrity of the study.

Noninvasive: When applied to a diagnostic device or procedure, means one that does not by design or intention: (1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os.

Non-Significant Risk (NSR) Device: A device that does not pose a significant risk to human subjects and one that does not meet the definition for an SR device.

Non-viable neonate: is a neonate after delivery that, although living, is not able to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Office for Human Research Protection (OHRP): An office within the United States Department of Health and Human Services (DHHS) that is responsible for implementing ethical oversight for clinical research.

Pharmacodynamics: describes the effects of the agent while in the body.

Pharmacogenomics: is the use of genetic information to predict whether a drug will help make a patient well or ill.

Pharmacokinetics: describes how the agent moves through and is excreted from the body.

Piedmont Healthcare Institutional Review Board (PHCIRB): The Piedmont entity local designated committee charged with responsibility to provide robust review, approval, and oversight monitoring of research to ensure the protection of the rights, safety, and well-being of human subjects participating in research.

Piedmont Healthcare Office of Research Services (ORS): The Piedmont entity designated office that oversees research activities occurring with Piedmont, facilitates research with affiliates, coordinates approvals, provides researcher training, and ensures that clinical research projects are conducted in a manner complaint with Piedmont policies and procedures.

Placebo is an inactive substance that looks the same as, and is administered in the same way as, a drug in a clinical trial.

Premarket Approval (PMA) is any type of premarket approval application used to obtain FDA approval of certain types of medical devices. It is the most stringent application for medical devices. The FDA approves a PMA if it determines that the application contains sufficient valid scientific evidence to provide reasonable assurance that the device is safe and effective for its intended use(s).

Principal Investigator: The lead scientist or scholar for well-defined research project.

Prisoner Representative: An individual representing the interests of incarcerated persons who may be approached and enrolled as research subjects.

Prisoner: 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 which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

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 which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (ie., a medical record). Private information must be individually identifiable in order for the obtaining of the information to constitute Human Subjects Research.

Protected Health Information (PHI): PHI is health information created or received by a covered entity or an employer that relates to past, present, or future physical or mental health

condition, provision of or payment for health care. PHI is any health information that identifies an individual. Individually identifiable health information that is created or received by a HIPAA-covered or hybrid entity.

Protocol: is the study plan that describes how a trial will be conducted including information about the investigational product, the criteria for subject selection, the schedule of procedures, and the plan for data analysis.

Protocol Deviation: A non-compliance with the study protocol and/or procedures that do not usually impact study participant rights, safety, and/or welfare, compromise the integrity of the study data and/or study participant willingness to participate in the study.

Protocol Violation: non-compliance with the study protocol and/or procedures that may impact study participant rights, safety, and/or welfare, the integrity of study data and/or study participant willingness to participate in the study.

Quality Assurance: planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and he applicable regulatory requirements.

Quorum: The minimum number of members that must be present to conduct official IRB business. A quorum is established when the following criteria are met: a) a majority of the voting IRB members are present (e.g., quorum for an IRB Committee of sixteen (16) voting members would be nine (9); (b) one of the voting members present is a non-scientist; and (c) if a protocol involving an FDA-regulated article is reviewed, then a licensed physician (MD) must be present.

Re-consenting: Notifying participants of changes in the research and documenting participants continued informed consent through signature or document research record that participant was informed verbally.

Recruitment: Process used by investigators to enroll appropriate subjects into a clinical trial.

Reportable Event: A process by which the investigator is to report any problem or event that qualifies for submission to PHCIRB.

Research: (1 – as defined by the DHHS): A clinical investigation or systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable 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.(2 – as defined by the FDA): Any experiment that involves a test article and one or more human subjects, and meets any one of the following:

a. must meet the requirements for prior submission to the FDA under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an

approved drug in the course of medical practice;

b. must meet the requirements for prior submission to the FDA under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR

c. any activity the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research marketing permit. A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Screen Failure: Participants who consent to participate in the project but who were disqualified during the screening process.

Serious adverse event: An event is considered serious if it results in death, is life-threatening, requires hospitalization or prolongation of hospitalization, causes persistent or significant disability or incapacity, is a birth defect or congenital malformation, represents, in the Principal Investigator's judgment, other significant hazards or potentially serious harm to research subjects or others, or any other event as described in the research protocol.

Serious non-compliance: Failure to act or willful violation of policies or regulations which create increased risk to research participants, adversely affects the rights, welfare and safety of research participants or adversely affects the scientific integrity of the study.

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.

'Short Form' is a written consent document stating that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative (LAR).

Significant risk device: 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 a use in 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.

Source Data: all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Source Document: is the initial documentation of data in a clinical study and includes recorded observations, laboratory reports, medical records, etc.

Sponsor: is the individual or company that initiates but does not actually conduct the investigation. The sponsor can be any legal entity, including a company, an academic organization, or an individual.

Sponsor-Investigator: means an individual who both initiates and conducts the clinical investigation and under whose immediate direction the investigational drug or device is being administered, used, or dispensed. The sponsor-investigator assumes all of the responsibilities of the sponsor as well as all the responsibilities of an investigator as outlined in the Form FDA 1572.

Study Personnel: Principal investigators, co-investigators, sub-investigators, research coordinators, and any other research team members who have contact with research participants and/or participants' research data and identifiers. Individuals whose primary contact with the participant is in the context of clinical care, but offer no additional role in research, are not considered key research personnel.

Sub-Investigator: an individual who is a member of the clinical trial team designated and supervised by the investigator to perform critical trial-related procedures and/or to make important trial-related decisions (for example, associates, residents, research fellows).

Subject: a human who participates in an investigation, either as an individual on whom or on whose specimen and investigational device or drug is used or as a control. A subject may be in normal health or may have a medical condition or disease.

Suspension: An action taken by the PHCIRB, PHCIRB Chair, or Institutional Official (IO) or designee to temporarily withdraw approval for some or all research activities in the interest of protecting research participants. Suspended protocols are considered open but may not continue enrollment or research activities that are not essential to the protection of research participants. The PHCIRB will advise researchers of the timing of the continuing renewal request requirement.

Systemic Investigation: An activity that involves a prospective research plan which incorporates data collection, either quantitative or qualitative, and data analysis to answer a research question.

Tabled: Postpone determination of approval. The IRB may require the investigator to make substantive changes to the protocol or informed consent documents, or submit clarifications or additional documents. The research may not proceed until the IRB reviews the revised research project and approves it at a subsequent convened meeting. Situation where the IRB cannot make the determination required for approval. The IRB may require the investigator to make substantive changes to the protocol or informed consent documents, or submit clarifications or additional.

Terminate/Terminations: The action taken by the PHCIRB to permanently withdraw approval for all research activities (excepting those activities required to protect research participants). Terminated protocols are considered closed and do not require a continuing renewal.

Test article: any drug for human use, 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 (Food and Drug Act).

Unanticipated Problem (involving risks to study subjects or others): to include any incident, experience, or outcome that meets **all** of the following criteria:

1. Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. Related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Withdrawals (Participant): Participants who signed the consent form, but later withdrew from the project. This does not include screen failures.

Withdrawals (Submissions): Items that are submitted via IRBNet that either were in error or did not qualify for prompt submission.

Working Agreement: Piedmont specific document that outlines which Piedmont services a researcher may utilize within the Piedmont entity for a research project.