Standard Operating Procedures  
Glossary of Terms

**510K:** A 510(k) Device is a new device that the FDA agrees is substantially equivalent to a device already on the market. 510(k) devices can be marketed without clinical testing. However, if clinical data are necessary to demonstrate equivalence, any clinical studies must be conducted in compliance with the requirements of the IDE, IRB review and informed consent regulations. Because 510(k) devices under clinical investigation fall under the IDE regulations, reporting of adverse or unanticipated 510(k) device effects will follow the same requirements.

**ADMINISTRATIVE HOLD:** A voluntary action by an investigator to stop research activities in a currently approved protocol.

**ADULT:** A person who has 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. Who is an adult may vary depending on the specific treatments or procedures involved in the research and on the jurisdiction in which the research will be conducted.

**ADVERSE DRUG REACTION (ADR):** In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out.

Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

**ADVERSE REACTION (Adverse Event – AE):** Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research. An adverse event encompasses both physical and psychological harms; and although they most commonly occur in the context of biomedical research, they can also occur in the context of social and behavioral research.

**ADVERTISEMENT:** Any form of communication aimed directly to potential research subjects and which is under the control of the investigator.

**ADVOCACY AND SUPPORT GROUPS:** Organizations and groups that actively support participants and their families with valuable resources, including self-empowerment and survival tools.

**ALLEGATION OF NON-COMPLIANCE:** An unproven assertion of non-compliance; suspected non-compliance with human subject protection regulations.

**AMENDMENT:** A revision, a change, or an addition (addendum) to an approved research protocol.

**ANONYMIZED:** Information (data) which does not contain any type of individual identifier, or any way that the information could be considered individually identifiable. Coded information (information that has a code, but no direct identifiers like name or birth date) is NOT considered anonymized.
APPLICABLE REGULATORY REQUIREMENTS: Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products of the jurisdiction where trial is conducted. (From FDA website)

APPROVED DRUGS: In the U.S., the Food and Drug Administration (FDA) must approve a substance as a drug before it can be marketed. The approval process involves several steps including pre-clinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application by the manufacturer of the drug, FDA review of the application, and FDA approval/rejection of application. (See Food and Drug Administration).

APPROVED PROTOCOL: Research which is approved by the IRB approved as submitted with no changes. Approval is usually for one year; however, under certain circumstances (e.g., in high risk studies in which the risks and benefits of the approved research cannot be fully anticipated) the IRB may limit the approval interval to a shorter period of time or require that the research be reviewed after a specific number of subjects are studied.

ASSENT: A child’s affirmative agreement to participate in research. Failure of a child to object to participation can not be construed as assent. Assent is a process involving communication with the child. A signature on an assent document is not, by itself, assent.

ASSURANCE: A written agreement that establishes standards for human subjects’ research as approved by the Office for Human Research Protections (OHRP) and is executed by the Institutional Official.

ARM: Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more. (See Randomized Trial).

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 requirement(s).

AUDIT CERTIFICATE: A declaration of confirmation by the auditor that an audit has taken place.

AUDIT TRAIL: Documentation that allows reconstruction of the course of events.

AUTHORIZATION: Permission to gain access to PHI. At UHCMC, Authorization for use and disclosure of PHI for research purposes is provided by signing a Research HIPAA Authorization Form, which provides clear descriptions of how privacy will be protected and confidentiality of the information.

BASELINE: 1. Information gathered at the beginning of a study from which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment which is being tested. At this reference point, measurable values such as CD4 count are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

BIAS: When a point of view prevents impartial judgment on issues relating to the subject of that point of view. In clinical studies, bias is controlled by blinding and randomization. (See Blind and Randomization).

BLINDING/MASKING: A procedure in which one or more parties to the trial are kept unaware of the
treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-
blinding usually refers to the subject(s), investigator(s), monitor, and in some cases, data analyst(s) being
unaware of the treatment assignment(s).

CASE REPORT: A case report, by UHCMC definition, is medical information collected and presented
on no more than three (3) patients to highlight an interesting treatment, presentation, or outcome. A case
report generally results from a retrospective review of the medical record and/or the clinical provider’s
files. In this regard, case reports differ from research protocols in which data are collected with intent to
evaluate a specific hypothesis.

CASE REPORT FORM (CRF): A printed, optical, or electronic document designed to record all of the
protocol-required information to be reported to the sponsor on each trial. (From FDA website)

CERTIFICATE OF CONFIDENTIALITY: A Certificate of Confidentiality is issued to protect
subjects’ privacy and ensure the confidentiality of their data. The Certificate prevents researchers from
having to release identifying information about human research subjects in any Federal, State or local
civil, criminal, administrative, legislative, or other proceedings. This protection is afforded by the Public
Health Service Act 301(d), 42 USC 241(d).

THE CLINICAL RESEARCH CENTER (CRC): A division of University Hospitals. The CRC
administratively oversees all active research at University Hospitals.

CHILD: A person, who has not attained the legal age for consent to treatments or procedures involved in
research, under the applicable law of the jurisdiction in which the research will be conducted.

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI): A web-based educational
program in the ethics of human subject research. It may be used for both core initial certification in the
CWRU CREC Program as well as continuing education requirements as required by UH.
www.CITIProgram.org

CLINICAL: Pertaining to or founded on observation and treatment of participants, as distinguished from
theoretical or basic science.

CLINICAL ENDPOINT: (See Endpoint).

CLINICAL INVESTIGATION: Any experiment that involves a test article and one or more human
subjects, and that is subject to the FDA regulations. FDA regulations consider the terms “clinical
investigation” and “research” to be synonymous. The following are considered experiments subject to
FDA regulations:
- Any use of a drug, other than the use of an approved drug in the course of medical practice.
- Any use of a medical device to evaluate safety or efficacy of that device.
- Any activity where data are being collection to submit to FDA or to be held for inspection by
  FDA.

CLINICAL INVESTIGATOR: A medical researcher in charge of carrying out a clinical trial's protocol.

CLINICAL TRIAL/STUDY: Any investigation in human subjects intended to discover or
verify the clinical, pharmacological, and/or other pharmacodynamic effects of an
investigational product(s), 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 safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

**CLINICAL TRIAL STUDY REPORT:** A written description of the trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report.

**CLINICAL TRIAL AGREEMENT:** A legally binding document identifying the obligations of the Sponsor, Principal Investigator and UHCMC. The terms of the agreement include, but are not limited to, payment/budget, confidentiality, indemnification, publication, insurance, adverse events, intellectual property, duration of the research, termination of research and governing laws.

**CLOSURE:** An action taken by an investigator to permanently discontinue research activities for a study that has current IRB approval.

**COGNITIVELY IMPAIRED:** Refers to an adult with a psychiatric disorder (e.g., schizophrenia, major depression, psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., dementia), a developmental disorder (e.g., mental retardation), or severe acute illnesses associated with cognitive impairment (e.g., stroke, seizure, metabolic coma, severe pain) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Depending on the illness, the impairment may be temporary, cyclical, or permanent.

**COHORT:** In epidemiology, a group of individuals with some characteristics in common.

**COLD CALLING:** When a person not known to the potential research subject contacts the subject without an introductory letter sent in advance of the call.

**COLLECTED TISSUE:** is any biological product (tissue, urine, gastric fluid, saliva, etc.) from a living human that is requested from the individual for the purpose of research.

**COMMUNITY-BASED CLINICAL TRIAL (CBCT):** A clinical trial conducted primarily through primary-care physicians rather than academic research facilities.

**COMPARATOR:** An investigational or marked product (i.e., active control), or placebo used as a reference in a clinical trial.

**COMPASSIONATE USE:** A method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug or therapy.

**COMPENSATION:** Payment for treatment of an unexpected adverse outcome that occurs during the research. It should not be used to refer to subject remuneration.

**COMPETENCE:** A legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Competence may fluctuate as a function of the natural course of an illness, response to treatment, effects of medication, general physical health, and other factors. Therefore, mental status should be re-evaluated periodically. As a designation of legal status, competence or
incompetence pertains to determination in court proceedings that a person's abilities are so diminished that his or her decisions or actions (e.g., writing a will) should have no legal effect. Such decisions are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

**COMPLEMENTARY AND ALTERNATIVE THERAPY:** Broad range of healing philosophies, approaches, and therapies that Western (conventional) medicine does not commonly use to promote well-being or treat health conditions. Examples include acupuncture, herbs, etc. (Internet Address: [http://www.nccam.nih.gov](http://www.nccam.nih.gov)).

**COMPLETED:** (See Recruitment Status).

**COMPLIANCE:** Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.

**CONFIDENTIALITY:** Prevention of disclosure, to other than authorized individuals of a sponsor’s proprietary information or of a subject’s identity.

**CONFIDENTIALITY REGARDING TRIAL PARTICIPANTS:** Refers to maintaining the confidentiality of trial participants including their personal identity and all personal medical information. The trial participants' consent to the use of records for data verification purposes should be obtained prior to the trial and assurance must be given that confidentiality will be maintained.

**CONFLICT OF INTEREST** or **CONFLICTING INTEREST:** the existence of one or more influences that might be strong enough to distract an IRB member from the IRB member’s primary duty. Conflicting interests are the ordinary factors that can influence judgment, such as personal relationships between an IRB member and an investigator, competition among departments, authority relationships, financial relationships, etc.

**CONTINUING NON-COMPLIANCE:** A pattern of non-compliance that, in the judgment of the IRB Chair or convened IRB, indicates a lack of understanding of the regulations or institutional requirements that may affect the rights and welfare of participants, would have been foreseen as compromising the scientific integrity of a study such that important conclusions could no longer be reached, suggests a likelihood that non-compliance will continue without intervention, or frequent instances of minor non-compliance. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance with human subject protection regulations.

**CONTINUING RESEARCH EDUCATION CREDITS (CREC) PROGRAM:** A Collaborative program through Case Western Reserve University (CWRU) which provides free and accessible documented training in the protection of human subjects in compliance with NIH research educational requirement.

**CONTINUING REVIEW:** Periodic review of research activities necessary to evaluate the progress of the study and to determine whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, and whether any new information regarding the risks and benefits should be disclosed to participants.

**CONTINUING REVIEW REMINDER NOTICES:** correspondences sent by the IRB to an investigator, as a reminder of the upcoming expiration of IRB approval of a protocol.
CONTRACT: A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.

CONTRACT RESEARCH ORGANIZATION (CRO): A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

CONTRAINDICTION: A specific circumstance when the use of certain treatments could be harmful.

CONTROL: A control is the nature of the intervention control.

CONTROL GROUP: The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo (See Placebo and Standard Treatment).

CONTROLLED TRIALS: Control is a standard against which experimental observations may be evaluated. In clinical trials, one group of participants is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo.

COVERED ENTITY: A health plan, a health care clearinghouse, or health care provider who transmits health information in electronic form in connection with a transaction for which DHHS has adopted a standard. A covered entity can be an institution, organization, or person. The covered entity is responsible for implementing Privacy Rule protections of Protected Health Information collected, generated, or stored under its auspices. University Hospitals and all related divisions, employees, and medical staff constitute a covered entity.

CREC: Continuing Research Education Credit

DATA CONFIDENTIALITY: refers to how the participant’s identifiable private information (data) will be handled, managed and disseminated

DATA SAFETY AND MONITORING BOARD (DSMB): An independent committee composed of community representatives and clinical research experts, that reviews data while a clinical trial is in progress to ensure that participants are not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

DECEPTION RESEARCH: When participants are intentionally misinformed or information is purposely held, as part of the research design.

DECISIONAL IMPAIRMENT: Refers to a limitation or incapacity that is not part of normal growth and development.

DEFFERED: A protocol is deferred when the changes proposed or questions raised by the Board are significant enough to warrant re-review of the protocol at a subsequent Board meeting. The investigator will receive notification of the issues the IRB needs addressed or changed. If a protocol is deferred it will usually be reconsidered by the same Board that deferred it. In addition to deferring the protocol the IRB may ask for additional review by expert consultants (IRB Policy, Membership), or it may refer the protocol for an ethics consultation (IRB Policy, UH Ethics Committee).
DE-IDENTIFIED: Information (data) which does not contain any direct individual identifiers, like name, address, birthdate, etc. Information that is coded is considered de-identified.

DEPARTMENT: is defined as one of the clinical or academic organizational units at UHCMC or in the Case School of Medicine, as well as selected Centers such as the Center for Global Health and the Ireland Cancer Center. For the purpose of this policy the definition also includes Schools such as the Frances Payne Bolton School of Nursing, and the Case School of Dentistry.

DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS) is the United States government's agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.

DEPARTMENT REVIEW COMMITTEES: committees within each academic and clinical Department at Case and UHCMC responsible for scientific review and approval of human subject research protocols prior to IRB review.

DIAGNOSTIC TRIALS: Refers to trials that are conducted to find better tests or procedures for diagnosing a particular disease or condition. Diagnostic trials usually include people who have signs or symptoms of the disease or condition being studied.

DIRECT ACCESS: Permission to examine, analyze, verify and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor’s monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects’ identities and sponsor’s proprietary information.

DISCARDED SPECIMEN: That portion of a collected specimen that is not needed for assessment of diagnostic, prognostic, and other parameters in the diagnosis and treatment of the patient. Discarded specimens include tissue, body fluids, urine, blood, and stool.

DISCARDED TISSUE: Any biological product (tissue, urine, gastric fluid, saliva, etc.) from a living human that is obtained during usual medical care which is of no further use in the medical care of the person and would otherwise be discarded.

DOCUMENTATION: All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

DOSE-RANGING STUDY: A clinical trial in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

DOUBLE-BLIND STUDY: A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study. (See Blinded Study, Single-Blind Study, and Placebo).

DOUBLE-MASKED STUDY: (See Double-Blind Study).

DRUG-DRUG INTERACTION: A modification of the effect of a drug when administered with another drug. The effect may be an increase or a decrease in the action of either substance, or it may be an adverse
effect that is not normally associated with either drug.

**EFFICACY:** (Of a drug or treatment). This is the maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the procedure mandated by the FDA, Phase II clinical trials gauge efficacy and Phase III trials confirms it (See Food and Drug Administration (FDA), Phase II and III Trials).

**ELIGIBILITY CRITERIA:** Summary criteria for participant selection; includes Inclusion and Exclusion criteria. (See Inclusion/Exclusion Criteria).

**EMERGENCY USE:** The use of an investigational drug, agent, device or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval.

**EMPIRICAL:** Based on experimental data, not on a theory.

**ENDPOINT:** Overall outcome that the protocol is designed to evaluate. Common endpoints are severe toxicity, disease progression, or death.

**ENROLLING:** This is the act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process.

**EPIDEMIOLOGY:** The branch of medical science that deals with the study of incidence and distribution and control of a disease in a population.

**ESSENTIAL DOCUMENTS:** Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

**ETHICS COMMITTEE:** refers to the UHCMC Ethics Committee, a committee of the Clinical Council.

**EXPANDED ACCESS:** Refers to any of the FDA procedures, such as compassionate use, parallel track, and treatment IND that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

**EXPECTED ADVERSE EVENTS:** Any event, the specificity or severity of which is consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is consistent with the risk information described in the general investigative plan or elsewhere in the current application, as amended

**EXPEDITED REVIEW:** Review of research involving human subjects by the IRB Chair, Vice-Chair, or by one or more experienced reviewers designated by the Chair from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110.

**EXPERIMENTAL DRUG:** A drug that is not FDA licensed for use in humans, or as a treatment for a particular condition (See Off-Label Use).

**EXPIRED STUDY:** continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. No activities can occur after the expiration date.
EXTERNAL (OFF-SITE) EVENT: Refers to an event reported to a UHCMC investigator that occurred in a participant who gave consent using consent documents that were not approved by the UHCMC IRB.

FEDERALLY ASSURED (FWA) is a written agreement that establishes standards for human subjects’ research as approved by the Office for Human Research Protections and is executed by the institutional official.

FETUS: The product of conception from implantation until delivery.

FINDER’S FEES: Money paid for recruiting subjects on a per subject basis.

FINDING OF NON-COMPLIANCE: Non-compliance determined by the IRB to be true.

FOOD AND DRUG ADMINISTRATION (FDA): An agency in the U.S. Department of Health and Human Services that is responsible for protecting the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products, medical devices, our nation’s food supply, cosmetics, dietary supplements, and products that give off radiation. It is responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices, including those used in the diagnosis, treatment, prevention, and research. The FDA also works with the blood banking industry to safeguard the nation’s blood supply. (Internet address: http://www.fda.gov).

FULL BOARD REVIEW: Review of research involving human subjects conducted by the full IRB Board at a convened meeting where quorum is present and is in accordance with the requirements set forth in 45 CFR 46.108.

GENERALIZABLE KNOWLEDGE: Knowledge "expressed in theories, principles, and statements of relationships" that can be widely applied to our experiences. The term "generalizable knowledge" is used to distinguish the results of research from the results of non-research activities such as clinical practice or teaching activities. For the most part, the terms clinical practice or teaching refer to interventions that are designed solely to enhance the well-being or knowledge of an individual.

GOOD CLINICAL PRACTICE (GCP): An international standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. It ensures that data reported are credible and accurate and that subjects’ rights and confidentiality are protected. The Good Clinical Practice Program is the focal point within FDA for issues arising in human research trials regulated by FDA.

GROUP PRACTICE: A group of physicians practicing the in the same specialty that uses a combined medical record facility and combined billing for professional services.

GUARDIAN: An individual, who is legally authorized under applicable state or local law, to consent on behalf of a child to general medical care.

HIPAA: The Health Insurance Portability & Accountability Act (HIPAA) enacted April 14, 2003. This regulation, also known as the “Privacy Rule”, establishes conditions under which researchers and investigators may have access to and use an individual’s PHI to for research purposes. This regulation indicates that signed authorization must be obtained unless the Institutional Research Privacy Board (RPB) has otherwise designated that this is not necessary.
HUMAN DATA: Information about humans that comes from a setting in which an individual can reasonably expect that no observation or recording is taking place or that the information will remain private. 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). Human data must be individually identifiable in order to be considered research involving human participants. This may include identifiable private information obtained from a primary participant about a third-party.

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

HUMANITARIAN DEVICE EXEMPTION (HDE): An application submitted to the FDA that is similar to a premarket approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD).

HUMAN SUBJECT (OR PARTICIPANT): As defined by DHHS: a human subject is 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 (45 CFR 46.102(f)). If the research involves a medical device, individuals are considered “subjects” when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812.3(p)).

As defined by FDA: 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 21 CFR 56.102(e). If the research involves a medical device, individuals are considered “subjects” when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR 812.3(p)).

HUMAN SUBJECT PROTECTION TRAINING: The UHCMC IRB requires human subjects’ protections certification of the Principal Investigator and all individuals listed on the study personnel table (co-investigators, coordinators, RNs, etc) of any research protocol regardless of funding; while Case’s policy on human subjects’ certification requires certification of the Principal Investigator and all key personnel, as defined by NIH, on all federally funded grants administered through Case. The UH IRB requires all investigators and study personnel who interact with subjects to be certified. In addition, the UH IRB certification requirements are applicable to research determined by the IRB to be exempt from IRB review and approval.

HYPOTHESIS: A supposition or assumption advanced as a basis for reasoning or argument, or as a guide to experimental investigation.

IDENTIFIABLE: Federal regulations define identifiable to mean that the identity of the individual subject is or may readily be ascertained by the investigator or may be associated with the information.

IMPARTIAL WITNESS: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject’s legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

IMPLANT: A device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also "implants" for purposes of this part.
INACTIVE PROTOCOL: A protocol where no participants have ever been enrolled at any site and no additional subject risks have been identified.

INCENTIVE: Refers to payment for time and discomfort.

INCLUSION / EXCLUSION CRITERIA: The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are based on such factors as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

INCOMPETENCE: A legal term meaning inability to manage one's own affairs. The term refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incapacity.

INDEPENDENT DATA MONITORING COMMITTEE (IDMC) (Also known as Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee): An independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

INDEPENDENT ETHICS COMMITTEE: An independent body of (a review board, or a committee, institutional, regional, national or supranational), constituted of medical/scientific professionals and nonmedical/nonscientific members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things reviewing and approving/providing favorable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of trial subjects. The legal status, composition, function, operations, and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guidance.

INFORMED CONSENT: An individual’s voluntary agreement, based upon adequate knowledge and understanding of the relevant information, to participate in research either for themselves or for a child for whom they are the parent or guardian (defined as an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

INFORMED CONSENT DOCUMENT (ICD): A document that describes the rights of the study participants, and includes details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document. The participant then decides whether or not to sign the document. Informed consent is not a contract, and the participant may withdraw from the trial at any time.

INSPECTION: The 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 (CROs) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).
**INSPECTIONAL OBSERVATIONS (FDA 483):** A 483 is a document issued when FDA investigators observe any significant objectionable conditions. The observations are cited when in an FDA investigator’s judgment these conditions or practices observed indicate that an FDA-regulated product is in violation of FDA’s requirements. The 483 does not constitute a final Agency determination of whether any condition is in violation of the Federal Food, Drug and Cosmetic Act or any of our relevant regulations.

**INTERIM CLINICAL TRIAL/STUDY REPORT:** A report of intermediate results and their evaluation based on analyses performed during the course of the trial.

**INSTITUTION:** Any public or private entity or agency or medical or dental facility where clinical trials are conducted.

**INSTITUTIONAL BIOSAFETY COMMITTEE (IBC):** the Case committee that is responsible for the review and approval of all human subject research protocols involving recombinant DNA.

**INSTITUTIONAL REVIEW BOARD (IRB):** is an administrative body established by a local institution to protect the rights and welfare of human subjects recruited to participate in research activities conducted under the auspices of the institution. A committee of physicians, statisticians, researchers, community advocates, and others that ensures that a clinical trial is ethical and that the rights of study participants are protected. All clinical trials in the U.S. must be approved by an IRB before they begin. Every institution that conducts or supports biomedical or behavioral research involving human participants must, by federal regulation, have an IRB that initially approves and periodically reviews the research in order to protect the rights of human participants.

**INTENT TO TREAT:** Analysis of clinical trial results that includes all data from participants in the groups to which they were randomized (See Randomization) even if they never received the treatment.

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

**INTERNAL (ON-SITE) EVENT:** An event (including unanticipated problems and adverse events) that occurs in a participant who was consented using a UHCMC IRB approved consent process. Studies approved by the IRB but conducted outside the United States are considered “on-site” for adverse event reporting.

**INTERVENTION:** Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects’ environment that are performed for research purposes.

**INTERVENTIONAL CLINICAL RESEARCH:** Any prospective study involving human subjects that is designed to answer specific questions about the effects or impact of a particular biomedical or behavioral intervention (i.e., drugs, devices, treatments or procedures, behavioral or nutritional strategies), or designed to answer specific questions about human physiology. These studies include research designed to evaluate the safety, effectiveness, or usefulness of therapies (e.g., drugs, diet, exercise, surgical interventions, or medical devices), diagnostic procedures (e.g., CAT scans or prenatal diagnosis through amniocentesis, chorionic villi testing, and fetoscopy) or preventive measures (e.g., vaccines, diet, or fluoridated toothpaste). Intervventional studies also include studies that include procedures with risk that are done solely for research purposes and of no benefit to the participant (e.g., bone marrow aspiration or bronchoscopy in normal volunteers).
INTERVENTION NAME: The generic name of the precise intervention being studied.

INTERVENTIONS: Primary interventions being studied: types of interventions are Drug, Gene Transfer, Vaccine, Behavior, Device, or Procedure.

INVESTIGATIONAL NEW DRUG (IND): A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous for purposes of this part. 21CFR 312.3.

INVESTIGATIONAL DEVICE EXEMPTION (IDE): An IDE allows the investigational device to be used in a clinical trial in order to collect safety and effectiveness data required to support a Pre-market Approval application (PMA) or a Pre-market Notification [510(k)] submission to the FDA. An IDE permits a device to be shipped lawfully for purposes of conducting investigations of that device. (21CFR 812.1). The FDA assigns each investigational device exemption (IDE) to either category A or B. All clinical investigations of devices must have an approved IDE or be exempt from the IDE regulation, see 21 CFR 812.2.

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

INVESTIGATOR: A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

INVESTIGATOR’S BROCHURE: A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects.

INVESTIGATOR INITIATED: The term refers to an individual who takes responsibility for, initiates, and conducts a clinical investigation at a single site. See also sponsor-investigator.

IRB AUTHORIZATION AGREEMENT: A formal agreement between UHCMC and another institution that allows the UHCMC IRB to serve as the IRB of Record for protocols at that institution.

IRB MEMBER: A person who is appointed as a member of the IRB with the right to participate in all discussions. A member of the IRB may be voting or non-voting.

IRB NON-VOTING MEMBER: A person who is appointed to the IRB with the right to participate in all discussions, but who does not vote or count in the quorum.

IRB OF RECORD: A term utilized when an institution assumes the IRB responsibilities for a human subject research protocol conducted at another institution. An IRB Authorization Agreement signed by institutional officials at

IRB VOTING MEMBER: A person who is appointed to the IRB with the right to vote and count in determining the quorum at a convened meeting.
**LEGALLY AUTHORIZED REPRESENTATIVE**: An individual, judicial or other entity 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. The term **legally authorized representative** may include a person properly appointed by an advanced directive (such as a living will or declaration) or a durable power of attorney for health care, certain court appointed guardians, and **next of kin** identified below in certain circumstances. Documentation of a person’s status as a **legally authorized representative** for a research subject is required and must be carefully evaluated to determine the validity of the appointment and scope, if any, of authority granted to make decisions regarding procedures involved in the research. For example, the existence of a durable power of attorney for health care or advanced directive for health care may not create a **legally authorized representative** for any or certain kinds of research decisions. The Law Department shall be consulted by the IRB and investigator if there are any questions related to **legally authorized representative** consent.

**LIFE-THREATENING EMERGENCY**: Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted.

**MAJOR PROTOCOL DEVIATION**: A more serious incident involving noncompliance with the protocol usually involving critical study parameters. Major protocol deviations generally affect the subject’s rights, safety, or welfare, or the integrity of the study data. A major protocol deviation can also be called a protocol violation.

**MASKED**: The knowledge of intervention assignment. (See *Blind*).

**MINIMAL RISK**: Both 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)).

**MINOR AMENDMENT**: A proposed change in research related activities that does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study.

**MINOR NON-COMPLIANCE**: Non-compliance that is neither serious nor continuing. An example of minor non-compliance includes failure to comply with UHCMC IRB policies that is administrative in nature (for example, turning in a report of an unanticipated problem a day late, failure to date a consent form or use of a consent form contextually identical to the IRB approved consent form, but without the presence of the IRB approval stamp).

**MINOR PROTOCOL DEVIATION**: An incident involving noncompliance with the protocol but one that typically does not have a significant effect on the subject’s rights, safety, welfare, or on the integrity of the resultant data.

**MONITOR**: An individual designated by a sponsor or contract research organization to oversee the progress of an investigation. The monitor may be an employee of a sponsor or a consultant to the sponsor, or an employee of or consultant to a contract research organization. *Monitor*, when used as a verb, means to oversee an investigation.

**MONITORING**: Reviewing a clinical study to ensure proper conduct, records and reports are performed as stated in the IRB approved protocol. It also involves the review of clinical research standard operating procedures, Good Clinical Practices, and regulatory requirements.
MONITORING REPORT: A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor’s SOPs.

MULTICENTER TRIAL: A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

NATURAL HISTORY STUDY: Study of the natural development of something (such as an organism or a disease) over a period of time.

NEONATE: A newborn.

NEW DRUG APPLICATION (NDA): An application submitted by the manufacturer of a drug to the FDA - after clinical trials have been completed - for a license to market the drug for a specified indication.

NON-COMPLIANCE: Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or the requirements or determinations of the IRB. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or more than once. The degree of non-compliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the noncompliance. Examples include, but are not limited to: Failure to obtain IRB approval; inadequate or non-existent procedures for the informed consent process; inadequate supervision; failure to follow recommendations made by the IRB; failure to report adverse events or protocol changes; failure to provide ongoing progress reports; or protocol deviations.

NON-INTERVENTIONAL STUDIES: Studies on normal human functioning and development that involve limited invasive or non-invasive procedures, e.g., blood or urine collection, moderate exercise, fasting, feeding, sleep, learning, responses to mild sensory stimulation, surveys or questionnaires, etc. are, for the purposes of this policy, considered non-interventional studies.

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. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered noninvasive.

NON-SERIOUS ADVERSE EVENT: Any event that causes interference with routine daily activities without major discomfort and these interferences do not persist. Non-serious events also includes events that are easily tolerated and do not affect participation in routine daily activities.

NON-STUDY RELATED EVENT: Refers to an event that would occur regardless of participation in the protocol.

NON-THERAPEUTIC RESEARCH: The research has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future.

NOTICE OF INSPECTION (FDA 482): An official notice from officers or employees designated by the FDA which is presented to the owner, operator, or agent in charge, authorizing: (A) to enter, at
reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers and labeling therein.

**OBSERVATIONAL STUDIES:** includes research that does not involve any intervention, alteration in standard clinical care or use in participants of any invasive or non-invasive procedure. Studies limited to the recording of data on individuals receiving standard medical care, the use of existing specimens or data, or the retrospective review of health information are, for the purposes of this policy, considered observational studies.

**OBTAINING DATA:** Receiving or accessing identifiable private information or identifiable specimens for research purposes.

**OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP):** The division of DHHS responsible for providing leadership on human research participant protections and implementing a program of compliance oversight for DHHS (45 CFR 46).

**OFFICE OF RESEARCH INTEGRITY:** The office within the Department of Health and Human Services that is responsible for investigating scientific misconduct and research integrity activities.

**OFF-LABEL USE:** The use of a FDA approved drug for a use that is not included in the approved label. This also includes the use of a drug for an approved illness or condition in an unapproved age group or at an unapproved dose.

**OPEN-LABEL TRIAL:** A clinical trial in which doctors and participants know which drug or vaccine is being administered.

**ORPHAN DRUGS:** An FDA category that refers to medications used to treat diseases and conditions that occur rarely. There is little financial incentive for the pharmaceutical industry to develop medications for these diseases or conditions. Orphan drug status, however, gives a manufacturer specific financial incentive to develop and provide such medications.

**PEER REVIEW:** Review of a clinical trial by experts chosen by the study sponsor. These experts review the trials for scientific merit, participant safety, and ethical considerations.

**PHARMACOKINETICS:** The processes (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

**PHASE I TRIALS:** Usually conducted in healthy volunteers; however, for more toxic drugs they are often done in patients who do not have any other approved or investigational treatment options. The goal is to determine what the most frequent side effects and, in some studies, how the drug is metabolized and excreted. The number of subjects typically ranges from 20 to 80. Treatment effects are not part of the assessment in phase 1 studies.

**PHASE II TRIALS:** Phase 2 studies begin if Phase 1 studies don't reveal unacceptable toxicity. While the emphasis in Phase 1 is on safety, the emphasis in Phase 2 is on effectiveness. This phase aims to obtain preliminary data on whether the drug works in people who have a certain disease or condition. For controlled trials, patients receiving the drug are compared with similar patients receiving a placebo or a
different drug. Safety continues to be evaluated, and short-term side effects are studied. Typically, the number of subjects in Phase 2 studies ranges from a few dozen to about 300.

**PHASE III TRIALS:** Phase 3 studies begin if evidence of effectiveness is shown in Phase 2. These studies gather more information about safety and effectiveness, studying different populations and different dosages and using the drug in combination with other drugs. The number of subjects usually ranges from several hundred to about 3,000 people.

**PHASE IV TRIALS:** Phase 4 studies occur after a drug is approved. They may explore such areas as new uses or new populations, long-term effects, and how participants respond to different dosages.

**PLACEBO:** an inactive substance that may resemble an active agent but has no medical value.

**PLACEBO CONTROLLED STUDY:** A trial in which treatment with a placebo is compared with treatment with a test drug. A placebo-controlled trial can be single blind, double blind, or open label.

**PLACEBO EFFECT:** A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change may be beneficial, reflecting the expectations of the participant and, often, the expectations of the person giving the substance.

**PRECLINICAL:** Refers to the testing of experimental drugs in the test tube or in animals - the testing that occurs before trials in humans may be carried out.

**PREGNANCY:** Encompasses the period of time from implantation until the end of pregnancy. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery. (45 CFR 46.202 Subpart B).

**PREVENTION TRIALS:** Refers to trials to find better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vaccines, vitamins, minerals, or lifestyle changes.

**PRINCIPAL INVESTIGATOR (PI):** An individual who actually conducts a clinical investigation, i.e., 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. The PI ultimately responsible for the conduct of the study and for assuring compliance with IRB policies and procedures and with Federal regulations.

**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. Ankle bracelets/in home restrictions are considered incarceration. Mental and substance abuse facilities are considered incarceration if someone is mandated to attend in lieu of jail or prison; however, an individual in such a facility is not considered incarcerated if they voluntarily commit themselves. Probation and parole are usually not considered as incarcerated.

**PRIVACY RULE:** Establishes the minimum Federal standards for safeguarding the privacy of individually identifiable health information (also referred to as protected health information (PHI)). The Department of Health and Human Services (DHHS) issued the Privacy Rule in order to implement the
Health Insurance Portability and Accountability Act of 1996 (HIPAA), which required compliance as of April 14, 2003 (see 45 CFR part 160 and subparts A and E of part 164). The Privacy Rule includes the standards for an individual’s privacy rights, to enable them to understand and control how their health information is used. Within DHHS, the Office for Civil Rights (OCR) is authorized to implement and enforce the Privacy Rule.

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 (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order to be considered information to constitute research involving human participants.

PROSPECTIVE RESEARCH: Utilizing human participants’ specimens/data that will be collected (in the future) after the research is approved by the IRB. Research involving medical records and ongoing collection of specimens for a tissue repository are examples of prospective research.

PROTECTED HEALTH INFORMATION (PHI): Individually identifiable health information, including demographic data that is collected from an individual, and:
1. is created or received by a health care provider, health plan, public health authority, employer, life insurer, school/university, or health care clearing house; AND
2. relates to past, present or future physical or mental health or condition of the 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
3. identifies the individual or where there is a reasonable basis to believe the information can be used to identify the individual; AND
4. is transmitted or maintained in any form or medium, whether electronic, paper or oral (see 45 CFR 160.103).

PROTOCOL: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guidance, the term protocol refers to protocol and protocol amendments.

PROTOCOL DEVIATION: Any alteration/modification to the IRB-approved protocol that is not approved by the IRB prior to its initiation or implementation.

PROTOCOL EXCEPTION: A temporary deviation from the protocol that has been approved by the IRB before its initiation. Protocol exceptions are usually for a specific participant (e.g., allowing enrollment of a participant who is close to, but outside of, the age eligibility).

QUALITY ASSURANCE (QA): All those 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 the applicable regulatory requirement(s).

QUALITY CONTROL (QC): The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial related activities have been fulfilled.
QUALITY IMPROVEMENT: A process by which individuals work together to improve systems and processes with the intention to improve outcomes. The primary goal is to improve care for specific populations, assessment and monitoring.

QUALITY OF LIFE TRIALS (or Supportive Care trials): Refers to trials that explore ways to improve comfort and quality of life for individuals with a chronic illness.

RANDOMIZATION: A method based on chance by which study participants are assigned to a treatment group. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant.

RANDOMIZED TRIAL: A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial. Occasionally placebos are utilized. (See Arm and Placebo).

RECRUITING: This is the period during which a trial is attempting to identify and enroll participants. Recruitment activities can include advertising and other ways of soliciting interest from possible participants. (See recruitment status and enrolling).

RECRUITMENT STATUS: Indicates the current stage of a trial, whether it is planned, ongoing, or completed. Possible values include:
- Not yet recruiting: participants are not yet being recruited or enrolled
- Recruiting: participants are currently being recruited and enrolled
- Enrolling by invitation: participants are being (or will be) selected from a predetermined population
- Active, not recruiting: study is ongoing (i.e., patients are being treated or examined), but enrollment has completed
- Completed: the study has concluded normally; participants are no longer being examined or treated (i.e., last patient's last visit has occurred)
- Suspended: recruiting or enrolling participants has halted prematurely but potentially will resume
- Terminated: recruiting or enrolling participants has halted prematurely and will not resume; participants are no longer being examined or treated
- Withdrawn: study halted prematurely, prior to enrollment of first participant.

REGULATORY DOCUMENTS: Documents that individually and collectively permit evaluation of the conduct of the study and the quality of the data produced.

REGULATORY AUTHORITIES: Bodies having the power to regulate. In the ICH GCP guidance, the expression "Regulatory Authorities" includes the authorities that review submitted clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities.

REIMBURSEMENT: Refers to payment for expenses incurred by study participants such as parking, transportation, or meals while participating in clinical research. Reimbursement out of pocket expenses related to research based on receipts provided by the research participant is not considered taxable income.

RENUMERATION: Any payment in dollars or items of value given to subjects participating in a study. It includes both reimbursement of expenses and payment for time and discomfort (incentives). It does not include study medications or supplies that are necessary for the conduct of the study. Remuneration may be considered taxable income to the research participant regardless of the dollar amount.
**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. Repositories are also referred to as tissue banks, collections, resources, inventories, or by other terms.

**RESEARCH:** As defined by DHHS any systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Under FDA regulations activities are “research” when they involve:

a. Use of a drug other than the use of an approved drug in the course of medical practice (21 CFR 312.3(b)).

b. Use of a medical device other than the use of an approved (means approved by the FDA for marketing) medical device in the course of medical practice (Food, Drug and Cosmetic Act 530(g)(3)(a)(i)).

c. Gather data will be submitted to or held for inspection by FDA in support of a FDA marketing permit for a food, including a dietary supplement that bears a nutrient content claim or a health claim, an infant formula, a food or color additive, a drug for human use, a medical device for human use, a biological product for human use, or an electronic product. (21 CFR 50.1(a) or 21 CFR 56.101(a)).

**RESEARCH INTEGRITY OFFICER (RIO):** The institutional official responsible for assessing allegations of scientific misconduct and determining when such allegations require an investigation.

**RESEARCH MISCONDUCT:** Fabrication, falsification, plagiarism in proposing, performing, or reviewing research, or in reporting research results.

**RESEARCH PRIVACY BOARD (RPB):** A review body which acts upon the HIPAA Privacy Rule’s authorization requirements for use or disclosure of PHI for a specific research protocol. The Research Privacy Board’s authority is limited to approval of privacy language; approval of requests for a waiver or alteration of the Privacy Rule’s authorization requirements; approval for the use of PHI from deceased individuals; and review of HIPAA compliance allegations. For UHCMC, the RPB consists of representatives from the IRB, the UH Privacy Office, UH Legal Department and the UH Center for Clinical Research.

**RESEARCH RECORD:** Recorded information in any medium, including paper, microfilm, magnetic tape, CDs, and any electronic form. Records include, but are not limited to original document, patient diaries, electronically-captured data, and letters and emails necessary for reconstruction of study conduct that are generated and/or received while conducting the human research project.

**RETROSPECTIVE RESEARCH:** Utilizing human participants’ specimens or data that were previously collected for other purposes before the research was approved by the IRB.

**RISK-BENEFIT RATIO:** The risk to individual participants versus the potential benefits. The risk/benefit ratio may differ depending on the condition being treated.

**SATELLITE FACILITIES/HEALTH CENTERS:** University Hospitals Health Centers contain medical laboratory and radiology services in a setting that combines the diagnostic and therapeutic services to furnish patients with comprehensive, compassionate patient care in one convenient location. The centers also provide access to specialists, including allergy and asthma, audiology and speech pathology, gastroenterology, obstetrics, gynecology, orthopedics, pain management,
SCIENTIFIC MISCONDUCT: Fabrication, falsification or plagiarism in proposing, performing or reviewing research or in reporting research results. It does not include honest error or honest differences in interpretation of data.

SCREENING: A process used to assess whether prospective subjects are appropriate candidates for inclusion in studies.

SERIOUS ADVERSE EVENTS (SAE): (21 CFR 312.32) Adverse events that result in any of the following outcomes: death; a life threatening experience; inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant disability/incapacity; or a congenital anomaly/birth defect. In addition, events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Although death is a serious adverse event, the reporting requirements are different.

SECONDARY RECRUITMENT: Asking a study subject for identifying information about friends or family members with the intent to contact them as potential additional research subjects.

SERIOUS NON-COMPLIANCE: An action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of participants, increases risks to participants, decreases potential benefits or compromises the integrity or validity of the research. Examples of serious non-compliance include, but are not limited to: Conducting non-exempt research without IRB approval; enrollment of subjects that fail to meet the inclusion or exclusion criteria of the protocol, that in the opinion of the IRB Chair, Vice Chair(s), or convened IRB increase the risk to the subject; or enrollment of research subjects while study approval has lapsed; or major protocol deviations that may place subjects at risk from the research.

SEVERELY DE佰ILITATING: 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.

SIDE EFFECTS: Any undesired actions or effects of a drug or treatment. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental drugs must be evaluated for both immediate and long-term side effects (See Adverse Reaction).

SINGLE-BLIND STUDY: This is a study in which one party, either the investigator or participant, is unaware of what medication the participant is taking (See Single-masked, Blind, and Double-Blind Study).

SINGLE-MASKED STUDY: (See Single-Blind Study).

SOURCE DATA: All information in 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 DOCUMENTS: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or
magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-
technical departments involved in the clinical trial).

**SPONSOR:** An individual, company, institution, or organization that takes
responsibility for the initiation, management, and/or financing of a clinical trial.

**SPONSOR-INVESTIGATOR:** An individual who both initiates and conducts, alone or with
others, a clinical trial, and under whose immediate direction the investigational product is
administered to, dispensed to, or used by a subject. The term does not include any person other
than an individual (e.g., it does not include a corporation or an agency). The obligations of a
sponsor-investigator include both those of a sponsor and those of an investigator.

**STANDARD TREATMENT:** A treatment currently in wide use and approved by the FDA, considered
to be effective in the treatment of a specific disease or condition.

**STANDARDS OF CARE:** Treatment regimen or medical management based on state of the art
participant care.

**STANDARD OPERATING PROCEDURES (SOP):** Detailed written instructions to maintain
standardization of a specific function.

**STATISTICAL SIGNIFICANCE:** The probability that an event or difference occurred by chance
alone. In clinical trials, the level of statistical significance depends on the number of participants studied
and the observations made, as well as the magnitude of differences observed.

**STUDY ENDPOINT:** A primary or secondary outcome used to judge the effectiveness of a treatment.

**STUDY RELATED EVENT:** Refers to an event that is related to participation in the protocol. The
event can be study-related or possibly study-related

**STUDY TYPE:** The primary investigative techniques used in an observational protocol; types are
Purpose, Duration, Selection, and Timing.

**STUDY WITHDRAWAL:** An action taken by the IRB to permanently withdraw a study, after it has
been reviewed and given contingent approval (minor modifications required to secure approval); or been
defered with a request for additional information for review, and the investigator does not respond.

**SUBJECT:** An individual who participates in a clinical trial, either as a recipient of the investigational
product(s) or as a control.

**SUBJECT IDENTIFICATION CODE:** A unique identifier assigned by the investigator to each trial
subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports
adverse events and/or other trial-related data.

**SUBJECT PRIVACY:** A person's desire to control the access of others to themselves. For example, a
person may not wish to be seen entering a place that might stigmatize them, such as a pregnancy
counseling center.

**SUSPENSION:** Research on an approved protocol is partially or completely stopped pending future
action by the IRB. Examples include: an unanticipated problem in research involving greater than
minimal risks to subjects or others; unexpected serious harm to subjects; or when the IRB is investigating a research protocol for possible issues of human subject non-compliance or continuing non-compliance with federal regulations, or with the determinations of the IRB. Suspended protocols remain open and require continuing review.

**TANGIBLE GIFTS:** Refers to items of nominal value (typically <$100 value) that are given to research participants (i.e. toy for a child participant, a tote bag or water bottle). Tangible gifts are not taxable.

**TERMINATION:** The IRB permanently stops some or all research procedures associated with an active approved protocol.

**TEST ARTICLE:** 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 FDA regulation.

**THERAPEUTIC RESEARCH:** Research involving testing an agent, procedure, or device for the eventual purpose of using the agent, procedure, or device to improve health or prevent disease in human subjects.

**TOXICITY:** An adverse effect produced by a drug that is detrimental to the participant's health. The level of toxicity associated with a drug will vary depending on the condition which the drug is used to treat.

**TREATMENT IND:** IND stands for Investigational New Drug application, which is part of the process to get approval from the FDA for marketing a new prescription drug in the U.S. It makes promising new drugs available to desperately ill participants as early in the drug development process as possible. Treatment INDs’ are made available to participants before general marketing begins, typically during Phase III studies. To be considered for a treatment IND a participant cannot be eligible to be in the definitive clinical trial.

**TREATMENT TRIALS:** Refers to trials which test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.

**UNANTICIPATED PROBLEM INVOLVING RISKS TO SUBJECTS:** Includes 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; and
2. 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.

**UNEXPECTED ADVERSE EVENTS:** (21 CFR 312.32) are defined as any adverse event, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigative plan (i.e., research plan) or elsewhere in the current application including the consent form, as amended. "Unexpected", as used in this definition, also refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.
**VULNERABLE SUBJECTS:** Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

**WAIVER OF ASSENT:** The assent plan and documentation of assent for minors must be recorded in the meeting minutes. The IRB will determine if the assent may be waived for all or some of the population, based on the justification provided by the investigator, and according to Federal regulations (45 CFR 46.408). This determination will be documented using the Federal citation number in the minutes of the Board meeting.

**WASHOUT PERIOD:** A period of time without active treatment, usually scheduled prior to initiation of placebo and active treatment arms. This can refer to a protocol required period of withdrawal from treatment before active treatment starts.

**WITHDRAWN:** (See Recruitment Status).