

Glossary of Terms

482: See *Notice of Inspection (FDA Form 482)*

483: See *Inspectional Observations (FDA Form 483)*

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.

1572: The Statement of Investigator (FDA Form 1572)

AAHRPP: See *Association for the Accreditation of Human Research Protection Programs*

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. For Ohio, an adult is 18 years or old. Although the FDA defines minors as persons aged 0-21 years, the IRB would not require parental permission for those ages 18-21 years of age (who are decisionally competent).

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 has been submitted to the IRB, reviewed by the IRB, and designated as meeting human subjects protection and regulatory requirements. There may be additional requirements unrelated to IRB review that must be completed before the research can begin. The period of approval will be assigned by the IRB.

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*).

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

ASSOCIATION FOR THE ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS (AAHRPP): Promotes high-quality research through an accreditation process that helps organizations worldwide strengthen their human research protection programs

(HRPPs). An independent, non-profit accrediting body, AAHRPP uses a voluntary, peer-driven, educational model to ensure that HRPPs meet rigorous standards for quality and protection. To earn accreditation, organizations must provide tangible evidence—through policies, procedures, and practices—of their commitment to scientifically and ethically sound research and to continuous improvement. As the "gold seal," AAHRPP accreditation offers assurances—to research participants, researchers, sponsors, government regulators, and the general public—that an HRPP is focused first and foremost on excellence.

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.

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*).

BIOREPOSITORY: A biological material repository that collects, processes, stores, and distributes biospecimens to support future scientific investigation.

BIOSPECIMEN: A sample of material, such as urine, blood, tissue, cells, DNA, RNA, or protein, from humans that may be used for a laboratory test or stored in a biorepository to be used for research.

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 COMPREHENSIVE CANCER CENTER (CCCC): A partnership organization supporting cancer-related research efforts at CWRU, University Hospitals Cleveland Medical Center, and Cleveland Clinic

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 ICH GCP E6R2 1.11)

CCCC: Case Comprehensive Cancer Center

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).

CERTIFIED COPY: A certified copy is a copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.

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

CHARGE DESCRIPTION MASTER (CDM or Charge Master): A comprehensive listing of items that could be billed to a patient or insurer by a healthcare provider. Its purpose is to develop an accurate summary of charges and services doctors and other healthcare professionals provide during the course of patient care.

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.

CENTER FOR IRB INTELLIGENCE (CIRBI): Advarra IRB software for submission and routing of applications for human subject protection review.

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI): A web-based educational program in the protection 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. See *Human Subjects Protections Training and Continuing Research Education Credits (CREC) Program*

CLAIM: Professional or technical list of clinical services, including lab charges, rendered for a patient that is used to invoice third party payors for payment.

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 RESEARCH: A project involving human subjects and participants that answer specific health questions or contribute to medical knowledge.

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 (CTA): 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 or the IRB 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 marketed 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>).

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 and certification 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. ICH GCP E6R2 1.20

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.

CORRECTIVE ACTION: Action taken to rectify a problem. *See Corrective and Preventative Action Plan (CAPA)*

CORRECTIVE AND PREVENTATIVE ACTION PLAN (CAPA): A quality process used to address an existing noncompliance issue and the steps taken to prevent further recurrence. Actions taken to collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence.

COVERAGE ANALYSIS (CA): Research Finance; A systematic review of all patient care procedures listed in a study protocol to determine which are allowable to bill to third party insurance. Non-billable services are budgeted for payment by the research study sponsor.

COVERED CHARGES: Services that can legally be billed to third party payors for payment. These services include: items that are otherwise available to a Medicare beneficiary, including items or services typically provided absent a clinical trial, items or services required solely for the provision of the investigational item, clinically appropriate monitoring of the effects of the investigational item/service or prevention of complications, and items or services for reasonable and necessary care arising from the provision of an investigational item or service. *Also see Non-Covered Charges*

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. *See Continuing Research Education Credits (CREC) Program*

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 clinical research experts and sometimes community representatives, 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. This is not a requirement of the IRB.

DATA USE AGREEMENT (DUA): An agreement that is required under the Privacy Rule and must be entered into before there is any use or disclosure of any data to an outside institution or party.

DATE OF SERVICE (DOS): The date that clinical services are provided to a patient, or the date that professional services are rendered (e.g.: radiology report)

DANGEROUS GOODS (DG): Articles or substances capable of posing a significant risk to health, safety or to property when transported by air.

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

DECISIONAL IMPAIRMENT: With respect to research and the informed consent process, decisional impairment means a diminished capacity to understand the risks and benefits of participation in research and thus to autonomously provide consent for participation. Decisional capacity is situation and study specific.

DEFERRED: A decision made when the IRB determines that the board is unable to approve research and the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB. If the IRB defers the human subjects research, a statement of the reasons for deferral and suggestions to make the study approvable will be provided. The study team may address the issues and resubmit. In most cases if the IRB's reasons for the deferral are addressed the human subjects research can be approved.

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 OF TRANSPORTATION (DOT): The US federal agency working under the authority of Congress to regulate the safe transportation of hazardous materials in intrastate, interstate, and foreign commerce.

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.

DISCLOSE: The release, transfer, provision of, access to, or divulgence of PHI to a person or entity *outside* UH. Also *Disclosure*.

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.

DUA: See *Data Use Agreement*

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*).

ELECTRONIC INVESTIGATOR SITE FILE (eISF): A computer system that may be used to house Essential Regulatory Documents required for the conduct of clinical research by the Investigator.

ELECTRONIC HEALTH RECORD (EHR): See *UHCare*

ELECTRONIC MEDICAL RECORD (EMR): See *UHCare*

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

EMAIL COMMUNICATIONS: Electronic Mail (“email”) means any message composed, sent or received by any person on the UH electronic mail systems and any attachments to such messages. Email communications, messages and documents are similar to paper documents and may be considered medical, business or other types of records that are subject to this policy. If a paper document must be retained in accordance with the UH retention schedule, an email message of the same content must be retained for the same length of time.

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.

EMERGENCY VARIANCE: In the event of an emergency, an already approved protocol or Standard Operating Procedure may diverge to keep patient safety a priority.

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.

ENROLLED: Generally means a research subject has been consented and screened, with eligibility verified. Also, Enrollment.

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.

EXEMPT HUMAN SPECIMEN: According to DOT and IATA regulations, Patient Specimens from a *non-infectious* human or animal are exempt from Infectious Substance regulations. These materials must be deemed non-infectious before they are classified as an exempt specimen. If there is suspicion that the material being transported contains a pathogen, it must be classified as an infectious material (either Category A or Category B).

- **While patient specimens are exempt from shipping requirements, packaging requirements must still be met (triple packing).**

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: In research, 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.

EXPORT ID: A TriNetX feature for re-identifying a de-identified patient list for recruitment. See *TriNetX*

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.

EXTERNAL USER: Personnel, not within the clinical trial team, including, but not limited to: an auditor, monitor, Sponsor, CRO, or CRA. The user is granted view-only access within a specific time-frame to maintain compliance with the monitoring review contract. External users should only be viewing de-identified information per UH IT permissions.

FEDERALWIDE ASSURANCE (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.

FIXED-COST CHARGES: Responsibility of Research Finance; Business costs to be charged that are consistent whatever the quantity of goods or services to be produced. E.g. study start-up fees, monitoring visit fees, non- patient care supplies, salary support, and annual fees.

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.

GENERAL EDUCATION MATERIALS: Materials created with the intent to provide general research education to patients, including (1) a definition of research; (2) what to expect when participating in research; (3) potential risks and benefits of participating in research; and/or (4) information about research the Department has conducted in the past. This material does not specifically intend to recruit patients and therefore, does not mention details or criteria of current research studies.

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 and reported results are credible and accurate and that subjects' rights, integrity, 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. ICH GCP E6R2 1.24

GRANT ACCOUNTANT (GA): Individual who performs all post-award functions. E.g. award setup, fixed cost invoicing, salary/non-salary charges, adjustments and cash application, etc.

GRANT ACCOUNTING INVOICE REQUEST FORM (GAIRF): Intake form which allows GA and Research Finance to invoice expenses that have been deemed recoverable.

GRANTS & CONTRACTS SPECIALIST (GCS): Individual who provides oversight of the legal and budget aspects of grants, including negotiation of adequate study budgets.

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.

Hazardous Materials (HM): Materials capable of posing an unreasonable risk to health and safety and property when transported in commerce.

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 8,000 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 all individuals listed on the study personnel table (PIs, co-investigators, coordinators, RNs, etc) of any research protocol regardless of funding; In addition, the UH IRB certification requirements are applicable to research determined by the IRB to be exempt from IRB review and approval. See *Continuing Research Education Credits (CREC) Program*

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.

IATA: *See International Air Transport Association*

IATA TRAINING: Department of Transportation training on the shipping and handling of hazardous materials. *See International Air Transport Association*

ICMJE: International Committee of Medical Journal Editors

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.

INFECTIOUS SPECIMENS (Class 6.2): Substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsiae, parasites and fungi) and other agents such as prions, which can cause disease in humans and animals. Infectious substances are further categorized into:

- **Infectious Substance Category A:** An infectious substance is one that is in a form that, when exposure to it occurs, is capable of causing permanent disability, life threatening or fatal diseases to humans or animals. These are subject to the strictest shipping requirements (special paperwork, labels, containers), whether in cultures or in human or animal specimens. Examples include, but aren't limited to, Ebola virus, Hepatitis B virus (cultures only) and West Nile virus (cultures only).
- **Biological Substance Category B:** All other infectious substances are classified as Category B infectious substances. These are still subject to the shipping regulations but with lesser requirements in terms of shipping papers and quality of containers.

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): *See Informed Consent Form*

INFORMED CONSENT FORM (ICF): 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 FORM 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.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA): Publishes the Dangerous Goods Regulations, which are instructions for transporting dangerous goods by air and are based on the International Civil Aviation Organization's (ICAO) Technical Instructions.

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): 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. ICH GCP E6R2 1.31

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.

INTERNATIONAL CONFERENCE ON HARMONISATION (ICH): Launched in 1990, ICH is a unique undertaking that brings together the drug regulatory authorities and the pharmaceutical industry and provides a unified standard for the European Union, Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in those jurisdictions.

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). Interventional 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 permitted by the U.S. Food and Drug Administration (FDA) to be tested in humans in a clinical investigation under the controls of a research protocol, but is not yet determined safe and effective for the indication studied to be legally marketed and sold in the United States for use in the general population. 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: Clinical devices that have not been cleared for marketing that involves an investigational plan approved by an institutional review board (IRB), informed consent from all patients, labeling stating that the device is for investigational use only, or is an approved device being used in a non- labeled indication.

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 (IP): A pharmaceutical form of an active ingredient, preventative (vaccine), therapeutic (drug or biologic), device, diagnostic, 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. ICH GCP E6R2 1.34

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 [RESEARCH]: The term refers to an individual who takes responsibility for, initiates, and conducts a clinical investigation at a single site. *Also see Sponsor-Investigator.*

INVESTIGATOR MANUAL FOR IRB SUBMISSIONS: Considered UH IRB Policy, the Investigator Manual for IRB Submissions offers guidance through policies and procedures related to the conduct of human subject research that are specific to the University Hospitals Cleveland Medical Center Institutional Review Board (UHCMC IRB). Investigators are required to abide by procedures as described in this manual. Also referred to as Investigator Manual and IRB Manual.

INVOICEABLE: Billable item which requires an invoice to the sponsor.

IRB AUTHORIZATION AGREEMENT (IAA): 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.

Generally, a formal, written agreement in which the reviewing IRB agrees to serve as the IRB of record for a relying institution, including an academic institution. Agreements are generally used to cover a single research study, categories of research studies or research studies within a research program

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 reviewing IRB that assumes IRB responsibilities for another institution and is designated to do so through an approved FWA on file with the Federal Office for Human Research Protections.

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.

LICENSED MEDICAL PROVIDER: An individual, such as a, physicians, nurse practitioners, or other health care professional with documented qualifications and/or licensure to perform medical related tasks (i.e. medical exam, review safety reporting, writing orders for procedures, prescribing medications, etc.). *See Medically Qualified*

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*).

MASTER FILE (MF): A collection of documents that must be produced in accordance with applicable international and local regulations containing essential documents that may be subject to regulatory agency oversight.

MATERIAL TRANSFER AGREEMENT (MTA): A contract that governs the transfer of tangible research materials between two organizations, when the recipient intends to use it for their own research purposes. It defines the rights of the provider and rights and obligations of the recipient with respect to the materials and any progeny, derivatives, or modifications.

MEDICAL: Connection with medicine or the practice or study of medicine

MEDICAL RECORD: Paper or electronic source document repository of care provided and patient status. Includes, but not exclusive of, the following: Allscripts Sunshine Enterprises [UHCare Ambulatory –Ambulatory Electronic Medical Record (aEMR)] & UHCare Acute– In Patient Electronic Medical Record; Community Record; Ensite; Mosaic (Radiology); Physician Portal. *See UHCare*

MEDICALLY QUALIFIED: Competent to practice medicine or perform medical procedures determined by education, training, experience, certification, license, or study of medicine.

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 are 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, contract research organization (CRO), or the UH Clinical Research Center to oversee the progress of an investigation to ensure the rights and well-being of human subjects are protected. Also to ensure that the reported trial data are accurate, complete, and verifiable from source documents and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s). 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: The act of overseeing or reviewing the progress of 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. ICH GCP E6R2 1.38

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. ICH GCP E6R2 1.39

MRN: Medical Record Number. See *UHCare*

MTA: See *Material Transfer Agreement*

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.

NCT NUMBER: National Clinical Trial (NCT) number, another term for the ClinicalTrials.gov registry number unique to each record. The format for the ClinicalTrials.gov registry number is “NCT” followed by an 8-digit number (e.g., NCT00000419).

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-COVERED CHARGES: Those services that must not be billed to third party payors. These services include: the investigational item or service itself (unless there is a coverage determination for that item or service), items and services provided by the research sponsors free of charge, items and services for data collection only. *Also see Covered Charges*

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 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 FORM 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.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION (OSHA): The main US federal agency charged with the enforcement of safety and health legislation.

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.

OHRP: *See Office for Human Research Protections (OHRP)*

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

OPERATING ROOM (O.R.): Facility where surgical operations are carried out in an aseptic environment. At University Hospitals this includes the following areas: Mather Outpatient Surgery Center aka “MOSC” (outpatient), Humphrey (women’s), Prentiss (pediatrics), and Mather (main O.R., adult).

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.

PATIENT CARE CHARGES: Expenses for items or services directly related to patient care.

PATIENT SPECIMEN: Human or animal materials, collected directly from humans or animals, including but not limited to excreta, secreta, blood and its components, tissue and tissue fluid swabs, and body parts being transported for purposes such as research, diagnosis, investigational activities, and disease treatment and prevention. Anything that is a therapeutic product is not considered a specimen, e.g., stem cells collected for treatment purposes.

- **Clinical Research Specimens** – (A subcategory of the definition of patient specimens developed for purposes of this SOP.) Specimens collected directly from humans including, but not limited to excreta, secreta, blood and its components, tissue and tissue fluid swaps, and body parts being transported for the purposes of research and investigational activities.

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.

PIPELINE AND HAZARDOUS MATERIALS SAFETY ADMINISTRATION (PHMSA): Division within DOT responsible with coordinating a national safety program for the transportation of hazardous materials by air, rail, highway and water.

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).

PREPARATORY TO RESEARCH: Activities that include preparing a research protocol, developing a research hypothesis, and ascertaining if there are a sufficient number of potentially eligible research participants.

PREVENTATIVE ACTION: Action taken to eliminate the root cause of a problem or potential problem including the detection/identification of issues. *See Corrective and Preventative Action Plan (CAPA)*

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.

PRIMARY COMPLETION DATE (PCD): The primary completion date is the date when the final subject was examined and/or received an intervention for the purposes of final collection of data for the pre- specified primary outcome (as per protocol), regardless of whether the clinical trial was completed (recruiting and data collection was completed per protocol), or terminated (recruiting or enrolling participants was halted prematurely and will not resume).

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 is 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.

PROCEDURE ROOM: Includes Cath Lab, EP Lab, as well as other departmental areas where devices may be implanted or provided to patients.

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): The 18 identifiable elements of personal information defined under the HIPAA law and relevant to any covered entity. PHI contains identifiers, insurance information, medical record number, physician, admission date or photographic images, for which there is a reasonable basis to believe the information can be used to identify a patient.

Any individually identifiable information of a person deceased more than 50 years is not PHI.

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).

PROTOCOL REGISTRATION AND RESULTS SYSTEM (PRS): ClinicalTrials.gov quality control and reviewing body to ensure all aspects of a clinical trial are entered according to federal regulations.

PTAEO: Post Award Grant Accounting Term (**P**roject, **T**ask, **A**ward, **E**xpenditure **T**ype, **O**rganization)

Q REQUISITION: (“Q” Requisition) UHLSF special study requisition used for outpatient research studies, which lists all covered labs required by a specific study. Labs listed on this requisition will be billed to patient insurance with a Q1 modifier, Z00.6 and condition code 30 placed on the claim for those claims sent to Medicare.

QUADAX (Xpeditor): A claim management system used to manage electronic transactions, featuring automated workflow, extensive conversion and editing capabilities, thorough audit trails for every transaction and full reporting. This is used specifically for viewing, editing and archiving patient claims.

QUALIFIED: Having the necessary or desirable qualities; fit; competent.

QUALIFIED PRESCRIBER FOR RESEARCH: A current state licensed prescriber who is able to prescribe drugs for humans in the state of Ohio, which is prescribing drugs within their

scope of practice for research protocols. The individual must be listed on the FDA 1572 form and on the IRB approval as a Co-Investigator.

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*).

RECORDS: Recorded information, regardless of medium or characteristic, which can be retrieved at any time. Records includes all original and non-identical copies of documents, any papers, forms, correspondence, x-rays, books, reproductions, cards, maps, photographs, blueprints, sound or video recordings, microfilm, visual aids, information on a computer, computer-generated materials (including tapes, backup tapes, CDs, disks, backup disks, diskettes and backup diskettes), or other documents (regardless of form) created or used to transmit or store information. Drafts or markups are not included (see below).

A. Entity business records include, but are not limited to, letterhead correspondence, legal opinions, real estate documents, directives and policies, official meeting minutes, personnel records, benefit programs, purchasing requisitions and invoices, accounts payable and receivable documents, tax documents, reimbursement documents, completed and signed forms, contracts, insurance documents, general ledgers, audit reports and financial reports.

B. Medical or patient records include, without limitation, clinical data as well as patient demographic information, clinical research and other information discovered or documented in the course of diagnosing and treating a patient.

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*).

[STUDY] RECRUITMENT MATERIALS: Any items that target patients with the intent to enroll them into particular research studies. This type of material requires submission to and approval from the IRB prior to use. Types of materials that fall under this category are: flyers, verbiage, brochures, social media post content, posters etc.

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.

REDCAP: REDCap (**R**esearch **E**lectronic **D**ata **C**apture) is a browser-based, metadata-driven electronic data software and workflow methodology for designing clinical and translational research databases.

REGULATORY BINDER: Compilation of essential regulatory documents related to a study. All studies conducted at University Hospitals are required to keep a regulatory binder.

REGULATORY DOCUMENTS: Regulatory/Essential documents that individually and collectively permit evaluation of the conduct of the study and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements

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.

RELIANT REVIEW: “Reliant Review” often referred to as “Facilitated Review” is a model that allows investigators to make a single Institutional Review Board (IRB) to serve as the “IRB of Record” for protocols conducted by any organization (or multiple organizations) while at the same time allowing each site to retain local context review and oversight. Through written contracts called “IRB Authorization Agreements (IAA)” participating institutions may allow Institution A to act as the “IRB of Record” for Institution B “Relying IRB”

RELIANT REVIEW FORM: A modified version of the UH IRB electronic smart form used for reliant studies.

RELYING IRB: “Relying IRB” is an Institutional Review Board with whom University Hospitals has entered into as part of a cooperative research project.

REMUNERATION: 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 BILLER NOTIFICATION FORM (RBNF): Document completed by departmental research staff to notify UHCRC team members of research patient visits.

RESEARCH FINANCE SPECIALIST (RFS): Individual who performs budgeting, billing reconciliation and invoicing of patient care charges. E.g. re-consent fees, as needed patient care charges, and serious adverse event reporting.

RFS IRF: Research Finance Specialist Invoice Request Form

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 PARTICIPANT COMPENSATION: Sponsor/Investigator approved monetary payment to research participants for their time, inconvenience, discomfort, or some other consideration as they relate to participation in a clinical trial.

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 collected for the purpose of human research protections. 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. Please refer to UH Policy GM-1-Records Management. (*Also see Records*)

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.

ROOT CAUSE: Factor that caused an issue or problem. *See Corrective and Preventative Action Plan (CAPA)*

ROOT CAUSE ANALYSIS: A class of problem solving methods used to identify the initial causes of problems or events. *See Corrective and Preventative Action Plan (CAPA)*

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, physical/occupational therapy, rheumatology, and urology. Additionally, some campuses have Urgent Care Centers or Surgery Centers on site.

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 DEBILITATING: 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*).

SOFT LAB AND SOFT AR MODULES: Information system responsible for laboratory result reporting and patient billing.

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). ICH GCP E6R2 1.51

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). ICH GCP E6R2 1.52

SPONSOR: An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial. ICH GCP E6R2 1.53

SPONSOR-INVESTIGATOR: An individual who both initiates and conducts, alone or with others, a clinical trial or investigation, 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 deferred with a request for additional information for review, and the investigator does not respond.

SUB-INVESTIGATOR: Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). ICH GCP E6R2 1.56. *See Investigator and Principal Investigator*

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.

SUNRISE: Software system for the operating room which incorporates supply management, documentation and billing capabilities.

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.

TRAVEL REIMBURSEMENT: Sponsor/Investigator approved reimbursement for travel expenses to and from the clinical trial site and associated costs such as mileage reimbursement, parking, transportation, meals, and lodging.

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.

TRINETX: A global health research network that brings together healthcare organizations, biopharmaceutical companies, and contract research organizations to optimize clinical research and enable discoveries through the generation of real-world evidence.

UH HONEST BROKER: The person from the Clinical Research Center who will receive the UH PI's request for information, re-identify the patients via TriNetX ExportID, and release the list to the investigator. Or, with requests for de-identified data, ensures that datasets are completely de-identified prior to release. See *TriNetX*

UHCARE: The electronic medical record system utilized by University Hospitals Health System. Also referred to as the electronic medical record (EMR) or electronic health record (EHR).

UHLSF: University Hospitals Lab Services Foundation.

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, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, which are likely to be vulnerable to coercion or undue influence, additional safeguards are to be included in the study to protect the rights and welfare of these subjects.

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*).

Z REQUISITION: ("Z" Requisition): UHLSF special study requisition used for outpatient research studies, which lists all non-covered labs required by a specific study. These labs will be charged to, and paid by, the study sponsor.