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 Investigational Device Exemption (IDE), Institutional Review Board (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

ADEQUATE TRAINING – Familiarity with the purpose of the study and the details of the protocol. Adequate understanding of the attributes of the investigational product needed to perform assigned tasks. Aware of the regulatory requirements and acceptable standards for the conduct of clinical trials and the protection of human subjects. Trained and competent as defined by licensure and the Principal Investigator (PI), research team lead, or clinical research education to perform the tasks they are delegated. Informed of pertinent changes during the conduct of the trial and receive additional training as appropriate.

ADMINISTER - the direct application of a drug, whether by injection, inhalation, ingestion, or any other means to a person.

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

ADULT: A person who has attained 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. The definition of 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 Texas, an adult is 18 years or older. Although FDA defines minors as persons aged 0-21 years, the IRB would not require parental permission for studies conducted in Texas for human subjects aged 18-21 years (who are competent to make their own decisions).

ADVERSE DRUG REACTION (ADR): All noxious and unintended responses to a medicinal product related to any dose during the pre-approval clinical experience with a new medicinal product or its new usages, particularly when the therapeutic dose(s) may not be established.

Regarding already marketed medicinal products: The World Health Organization (WHO) defines an ADR as any 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 or claim that an action (or an omission) does not conform with established regulations, policies or procedures; a claim of failure to meet human subject protection regulations.

AMENDMENT: A revision, change, deletion, modification, 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 date of birth) is NOT considered anonymized.

APPLICABLE CLINICAL TRIALS: As defined by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA). These are defined as:

- Interventional studies;
- Studies involving drugs, biologics, or medical devices regulated by FDA;
- Studies that require an IND or IDE;
- Studies that one or more of the following applies:
- At least one site in the US or its territories, or

- The product is manufactured in and exported from the US or one of its territories.
- Studies that are not Phase I (drug and biological products) or not Device Feasibility (device products)

Applicable clinical trials are subject to federal registration requirements and results reporting at the federal website ClinicalTrials.gov.

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 (NDA) by the manufacturer of the drug, FDA review of the application, and FDA approval/rejection of application. (See Food and Drug Administration)

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

ASSENT: A minor's affirmative agreement to participate in research. Failure of a minor to object to participation cannot be construed as assent. Assent is a process involving communication with the minor. 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 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: See Federalwide Assurance for the Protection of Human Subjects (FWA)

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 occurred.

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

AUTHORIZATION: (also known as Privacy Rule Authorization or HIPAA Authorization for Research): An Authorization is an individual's signed permission to allow a covered entity under HIPAA to use or disclose the individual's protected health information (PHI) that is described in the Authorization for the purpose(s) and to the recipient(s) stated in the Authorization. In contrast, an informed consent document is an individual's agreement to participate in the research study and includes a description of the study, anticipated risks and/or benefits, and how the confidentiality of records will be protected, among other things. An Authorization can be combined with an informed consent document or other permission to participate in research. If a covered entity obtains or receives a valid Authorization for its use or disclosure of PHI for research, it may use or disclose the PHI for the research, but the use or disclosure must be consistent with the Authorization.

At UTRGV, 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. This language may also be included in within the Informed Consent Form.

AUTHORIZED PRESCRIBER: As defined by the Texas Board of Pharmacy and Texas Medical Association – is a licensed health professional authorized to prescribe drugs.

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 vital signs and lab values are recorded. Safety and efficacy of a drug are often determined by monitoring for changes from the baseline.

BIAS: When a point of view prevents impartial judgment on issues regarding that point of view. Bias can occur at any phase of the research, including study design or data collection, as well as in the process of data analysis and publications. In clinical studies, bias is controlled by blinding and randomization. (See Blinding/Masking and Randomization)

BIOREPOSITORY: A biological material repository that collects, stores, and manages distribution of 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).

BLOODBORNE PATHOGENS (BBP): Pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to, hepatitis B virus (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV).

CASE REPORT: A case report, by UTRGV 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 the 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)

CENTER FOR MEDICARE AND MEDICAID SERVICES (CMS): The organization that administers Medicare and Medicaid benefits and federal regulations of the programs, including the CMS Clinical Trial/Research Policy NCD 310.1 and the guideline for clinical research billing, Medicare Claims Processing Manual Chapter 32, section 69.

CERTIFICATE OF CONFIDENTIALTY: A Certificate of Confidentiality is issued by the National Institutes of Health (NIH) and other Department of Health and Human Services (HHS) agencies to protect identifiable research information from forced or compelled disclosure. The Certificate allows the investigator and others who have access to research records to reuse to disclose identifying information about human research subjects in civil, criminal, administrative, legislative, or other proceedings, whether federal, state or local. This protection is afforded by the Public Health Service Act 301(d), 42 USC 241(d).

Certificates of Confidentiality protect subjects from compelled disclosure of identifying information but do not prevent the voluntary disclosure of identifying characteristics of research subjects. Researchers, therefore, are not prevented from voluntarily disclosing certain information about research subjects, such as evidence of child abuse or a subject's threatened violence to self or others. However, if a researcher intends to make such voluntary disclosures, the consent form should clearly indicate this. Furthermore, Certificates of Confidentiality do not prevent other types of intentional or unintentional breaches of confidentiality.

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.

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.

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 either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic (FD&C) Act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the FD&C Act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies (FDA, CFR - Code of Federal Regulations Title 21, n.d.).

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

CLINICAL RESEARCH: the National Institutes of Health (NIH) defines clinical research as: (1) patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. Patient-oriented research includes: (a) mechanism of human disease; (b) therapeutic interventions; (c) clinical trials; or (d) development of new technologies. (Excluded from this definition are *in vitro* studies that utilize human tissues that cannot be linked to a living individual.); (2) epidemiologic and behavioral studies; or (3) outcomes research and health services research.

CLINICAL RESEARCH ORGANIZATION (CRO): An entity that assumes one or more of the obligations of the Sponsor, as an independent contractor to the Sponsor.

CLINICAL TRIAL/STUDY: A research study performed in people that are aimed at evaluating a medical, surgical, or behavioral intervention. These studies test new ways to prevent, detect, or treat a disease. Treatments may be new drugs or combination of drugs, new surgical procedures or devices, or new ways to use existing treatments. Clinical trials also test other aspects of care, such as ways to improve the quality of life for people with a chronic health problem.

CLINICAL TRIAL AGREEMENT (CTA): A legally binding contract between UTRGV and a sponsor that describes the obligations of the parties with regards to the conduct of a clinical trial/study. Agreement terms and conditions 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.

CLINICAL TRIAL/RESEARCH FINANCIAL ANALYST (CTFA): The analyst is designated to perform the Coverage Analysis process for all applicable research projects.

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.

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

CODED INFORMATION/DATA: Data separated from personal identifiers through use of a code. As long as a link exists, data are considered indirectly identifiable and not anonymous or de-identified.

COERCION: Occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance or research participation. For example, an investigator telling a prospective subject that he or she will lose access to needed health services if he or she does not participate in the research (OHRP, n.d.).

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 affect cognitive or emotional functions to the extent that capacity for judgement 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.

COLLABORATIVE INSTITUTIONAL TRAINING INITIATIVE (CITI): A web-based educational program in the protection of human subject research. Modules are required to be completed by research personnel conducting research at UTRGV and affiliated sites. The Division of Research Integrity & Compliance (DRIC), in conjunction with the CITI Program, has made available online courses in Human Subject Protections, Responsible Conduct of Research, Laboratory Animal Welfare and Good Clinical Practice.

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

COMMON TERMINOLOGY CRITERIA for ADVERSE EVENTS (CTCAE) – A descriptive terminology which can be utilized for Adverse Event (AE) reporting developed by the National Cancer Institutes (NCI). A grading (severity) scale is provided for each AE term.

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

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

COMPASSIONATE USE: A method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options and are not eligible for participation in a clinical trial that offers the experimental therapeutics. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug or therapy.

COMPENSATION: Payment(s) made to cover the medical treatment of an unexpected adverse outcome that occurs as an outcome of the research. Compensation is not the same as 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.

COMPLETED: (See Recruitment Status).

COMPLIANCE: Adherence to trial-related requirements, good clinical practice (GCP) requirements, and applicable, policies, procedures, statutes and regulatory requirements.

CONCOMINANT MEDICATIONS: Prescription medications, over the counter drugs or dietary supplements that a clinical trial participant happens to be taking at the time of the trial, in addition to the drug under investigation. Also called Con-meds.

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

CONFIDENTIALITY DISCLOSURE AGREEMENT (CDA): A legal document which ensures confidentiality of proprietary information that a sponsor gives to an investigator. A signed, study specific CDA may be required before a sponsor will provide its proprietary information,

such as the study protocol to an investigator. It is also referred to as a Non-Disclosure Agreement (NDA) or Confidentiality Agreement. The agreements are signed by the Institutional Official after legal review has occurred. PIs are not allowed to sign these documents.

CONFIDENTIALITY REGARDING TRIAL PARTICIPANTS: Refers to maintaining the confidentiality of trial participants including their personal identity and all personal medical information. The trial participant's 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, Principal Investigator or Sub-Investigator from their primary duty. Conflicting interests are the ordinary factors that can influence judgment, such as personal relationships between an IRB member and investigator, investigator and sponsor, competition among departments, authority relationships, financial relationship, etc.

CONTINUING NON-COMPLIANCE: A pattern of non-compliance that, in the judgement 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 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: Correspondence 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 the contract.

CONTRACT RESEARCH ORGANZIATION (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

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

CONTROLLED DOCUMENT: A document is "controlled" when it must undergo formal review, formal approval, controlled distribution, controlled modification and controlled storage and access.

CONTROL GROUP: The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo.

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.

COPY: Duplication of a primary document without any certification attached to it. See Certified Copy definition.

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

CORRECTIVE AND PREVENTIVE ACTION PLAN (CAPA): A quality process used to address any existing noncompliance issue and the steps taken to prevent further recurrence. Actions taken to collect 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): A uniform method of analyzing the items and services provided in a clinical trial to determine if that item or service can be appropriately billed to Medicare and other insurers. A two-part process: 1) determining if it is a covered trial per Medicare NCD 310.1 guidelines and 2) developing the billing matrix -designating all services as either "research" or "routine cost" services. The process takes into consideration published practice guidelines, Local Coverage Determinations (LCD) and National Coverage Determinations (NCD). Through this process both a Qualification Form and Billing Matrix are produced.

COVERAGE ANALYSIS BILLING MATRIX: A detailed spreadsheet identifying and itemizing all possible health system charges generated within the research project that are identified in the research project protocol, including the time points at which each service will take place and the responsible financial payer of each service and time point listed.

COVERAGE ANALYSIS QUALIFICATION FORM (QF): A detailed form, listing the CMS criteria for a qualifying research project, used to document and attest that a project meets all required criteria of qualifying clinical research based on CMS NCD 310.1. The document includes the required qualifying criteria, which of the criteria the research project meets, and final determination of the project as a qualifying or non-qualifying research project.

COVERED CHARGES: Services that can be legally 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 the 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. UTRGV, all health-related divisions, employees, and medical staff constitute a covered entity.

CURRENT PROCEDURAL TERMINOLOGY (CPT) CODES: CPT Codes offer doctors, researchers and healthcare professionals a uniform language for coding medical services and procedures to streamline reporting, increasing accuracy and efficiency.

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

DATA CLARIFICATION FORM (DCF): A document that requests additional information and/or clarification of data entered on a specific case report form and with its completion with dated signature(s) serve as confirmation, clarification and/or correction of the original data entry.

DATA SAFETY 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 DRUG: As defined by the Texas Board of Pharmacy, any drug or IP that requires a prescription for possession or administration to a patient.

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 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 or redacted is considered de-identified.

DEPARTMENT: One of the clinical or academic organizational units at UTRGV.

DEPARTMENT OF HEALTH AND HUMAN SERVICES (DHHS): The United States government's agency for protecting the health of all Americans and providing essential human services, especially 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 UTRGV 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: The 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/DISCLOSURE: The release, transfer, provision of, access to, or divulgence of PHI to a person to entity *outside* UTRGV.

DISPENSE: The final association of a drug with a particular research participant pursuant to the prescription, drug order, or other lawful order of a prescriber and the professional judgement of and the responsibility for: interpreting, preparing, compounding, labeling, and packaging a specific drug.

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 placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and participant about the experimental drug do not affect the outcome; also called double-masked study.

DOUBLE-MASKED STUDY: See Double-Blind Study

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

EFFICACY: (Of a drug or treatment). This is the maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested 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 confirm it (See Food and Drug Administration (FDA), Phase II and III Trials).

ELECTRONIC CASE REPORT FORM (eCRF): Auditable electronic record designed to capture information required by the clinical trial protocol to be reported to the sponsor on each trial subject. A CRF in which related data items and associated comments, notes, and signatures are linked electronically.

ELECTRONIC INVESTIGATOR 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): Digital versions of patient medical records both historical and current. This includes, but is not limited to, medical history, diagnoses, medications, treatment plans, immunizations, allergies, radiological images, laboratory results, hospital records, notes and records from clinicians and caregivers, and clinical trial involvement. Records can be uploaded or scanned from a paper format or created originally within an EHR system. Also referred to as Electronic Medical Record (EMR).

ELECTRONIC MEDICAL RECORD (EMR): See definition for Electronic Health Record

ELECTRONIC PROTECTED HEALTH INFORMATION (ePHI): Information that is transmitted by electronic media or maintained in any electronic storage media including memory devices in computers (hard drives) and any removable/transportable digital memory medium, such as magnetic tape or disk, optical disk, or digital memory card.

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

EMERGENCY USE: The use of an investigational drug, agent, device, or biological product with 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 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 per protocol, with eligibility verified. Also, see Enrolling.

ENROLLING/ENROLLMENT: This is the act of signing up participants into a study. 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 data produced.

ETHICS COMMITTEE: Synonymous with the UTRGV IRB.

EXEMPT HUMAN SPECIMEN: According to DOT and IATA regulations, patient specimens for which there is minimal likelihood and pathogens are present are not subject to these regulations if the specimen is packed in a packaging which will prevent any leakage, and which

is marked “Exempt human specimen”. 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 infectious material (either Category A or Category B). *While patient specimens are exempt from shipping requirements, packing requirements must still be met (triple packing).*

EXEMPT STUDY: research activities in which the only involvement of human subjects will be in one or more of the exempt categories defined by the federal regulations. Exempt studies are exempt from some parts of the federal regulations but still subject to institutional policies and compliance.

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 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 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. Expedited research includes minimal risk to participants but does not fulfill the criteria for exemption.

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 approved study period specified by the IRB. IRB approval expires automatically. No study related activities can occur after the expiration date or during a lapse in approval dates.

EXTERNAL (OFF-SITE) EVENT: An event that occurs to a research participant enrolled at a study site under the jurisdiction of another IRB at another institution (non-UTRGV or UTRGV-Affiliate). A summary of these events will be submitted to the UTRGV IRB at the time of continuing review.

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 specified time frame to maintain compliance with the monitoring review contract. External users should only be viewing de-identified information per UTRGV permissions unless otherwise necessary for the integrity of the research and agreed to by the participant during the informed consent and research HIPAA consent.

FEASIBILITY ASSESSMENT: To evaluate the possibility of conducting a clinical trial in a proposed location based on a list of questions. The answers will allow the sponsor (if applicable) and/or a qualified PI to make an informed decision regarding the feasibility of the study at his/her site.

FEDERALWIDE ASSURANCE (FWA): A written statement whereby an institution commits to the Department of Health and Human Services (HHS) that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR Part 46 whenever it engages in human subjects' research. The Federalwide Assurance is the only type of assurance accepted and approved by the HHS Office for Human Research Protections (OHRP).

Institutions must have an FWA in order to receive HHS support for research involving human subjects' research.

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, monitor or auditor to be true.

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

FLORENCE eBINDERS™/eISF: a 21 CFR Part 11 compliant software used by UTRGV for electronic regulatory and remote monitoring/auditing.

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.

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

FUNDING SOURCE: The organization or funding agency that funds a clinical research project. This may include an industry sponsor, grant, department funds, etc.

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

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

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

HAZARDOUS MATERIALS: Materials capable of posing an unreasonable risk to health and safety and property when transported in commerce.

HEALTHCARE COMMON PROCEDURE CODING SYSTEM (HCPCS): A collection of standardized codes that represent medical procedures, supplies, products and services. The codes are used to facilitate the processing of health insurance claims by Medicare and other insurers.

HEALTHCARE LICENSE – An agency – or government granted permission issued to a health care professional to engage in a given occupation on finding that the applicant has attained the degree of competency and met educational requirements necessary to ensure public safety.

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 for research purposes. This regulation indicates that signed authorization must be obtained unless the IRB 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 USE EXEMPTION: 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 8123(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, the 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 UTRGV 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 UTRGV IRB certification requirements are applicable to research determined by the IRB to be exempt from IRB review and approval.

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

IDENTIFIABLE: Federal regulations define identifiable to mean that the identity of the individual subject is or may be readily 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.

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".

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 standard 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 the nonmedical/nonscientific member, whose responsibility 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 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 Committees to act in agreement with GCP as described in this guidance.

INFECTIOUS SUBSTANCES (Class 6.2): Substances which are known or are reasonably expected to contain pathogens. Pathogens are defined as micro-organisms (including bacteria, viruses, rickettsia, 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 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 are not 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 also includes the process by which the individual obtaining consent ensures potential participants have a consent in their primary language, have any legal guardians, translators or witnesses present (if applicable), have adequate time to review, are consented in a private setting, are capable of providing consent, are able to understand the consent form, are aware of any risks inherent to participating in the research, are not subject to coercion and are given copies of the consent form(s).

INFORMED CONSENT DOCUMENT: 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 authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or at the 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 judgement, 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 a 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 the International Civil Aviation Organization's (ICAO) Technical Instructions.

INTERNATIONAL AIR TRANSPORT ASSOCIATION (IATA) TRAINING: Department of Transportation training on the shipping and handling of hazardous materials.

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

INSTITUTIONAL BIOSAFETY COMMITTEE (IBC): The committee responsible for the review and approval of all human subject research protocols that involve, but are not limited to, recombinant DNA, RNAi, pathogens, human materials and other potentially infectious materials as well as transgenic animals. The IBC provides recommendations to the intramural community in matters pertaining to the control of biohazards associated with the use of microbiological agents and their vectors.

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 ensure the that a clinical trial is ethical, and 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: 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: Any unfavorable event related to the research procedure(s)that occurs to a UTRGV research participant in a study approved by the UTRGV IRB (both single site and multi-center) and that has a UTRGV or UTRGV Affiliate institution's faculty, staff, or student acting as Principal Investigator. Studies approved by the IRB but conducted outside the United States are considered "on-site" for adverse reporting.

INTERNATIONAL CONFERENCE ON HARMONIZATION (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., CT 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 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 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 the purposes of conducting investigations of that device. (21 CFR 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 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 to be safe and effective for the indication 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. 21 CFR 312.3

INVESTIGATIONAL PHARMACIST: An investigational pharmacist is responsible for the receipt, storage, accountability, dispensing, and return/destruction of all investigational drugs.

INVESTIGATIONAL PRODUCT (IP): A pharmaceutical from an active ingredient, preventive (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, one investigator is the responsible leader of the team and may be called the principal investigator. (ICH GCP E6R2 1.34

INVESTIGATOR'S BROCHURE: A collection of all relevant information known prior to the start-up of a clinical research study involving an investigational product (s). It includes the pre-clinical data such as chemical, pharmaceutical, toxicological, pharmacokinetic and pharmacodynamic data in animals and humans as well as the results of earlier trials.

INVESTIGATOR INITIATED RESEARCH: The term refers to a research protocol developed and initiated by 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 by UTRGV 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 UTRGV 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 UTRGV and another institution that allows UTRGV 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 (OHRP).

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.

KEY PERSONNEL: An individual designated by the principal investigator who is knowledgeable about the research study. This may include investigators, coordinators, assistants, residents, fellows, students working on the research, administrators or managers who oversee the research, and external individuals associated by agreement or contract with UTRGV Health who are involved in conducting the research. Individuals providing services in the course of their position (e.g., pharmacist, biostatistician) are not considered key personnel unless involved in key aspects of the research such as protocol development, consenting, blinding procedures etc.

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 durable power of attorney for healthcare, 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.

LICENSED MEDICAL PROVIDER: An individual, such as 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 or condition 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.

MASTER FILE/TRIAL MASTER FILE (MF/TMF): 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 RECORD: Paper or electronic source document repository of care provided and patient status.

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-noncompliance includes failure to comply with UTRGV 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 non-compliance with the protocol but one that typically does not have a significant effect on the subject's rights, safety, welfare, or the integrity of the resultant data.

MONITOR: An individual designated by a sponsor, contract research organization (CRO), or UTRGV research administration 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 or consultant to a sponsor, an employee of or consultant to a CRO, or an employee of or consultant to UTRGV research compliance department. 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 reporting is 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 and site Principal Investigator 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

MTA: 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.

NATIONAL INSTITUTE OF STANDARDS and TECHNOLOGY (NIST): A non-regulatory federal agency within the U.S Department of Commerce. NIST's mission is to promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life.

NATURAL HISTORY STUDY: Study of the natural development of something (such as an organism or 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: Newborn

NETWORK ID: An account provided by UTRGV required to gain access to UTRGV network applications.

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 or IBC. 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 non-compliance. 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 involved 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.

NON-INVASIVE: 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 non-invasive, 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 non-invasive.

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

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.

NOTE-TO-FILE: A description of the protocol specific method of accomplishing a process. This document can also be used to describe the reason for a discrepancy, missing data or missing documentation or to clarify information that may be otherwise unclear in regulatory or source documents (list of legal names of site(s) or staff, location of central files, etc.)

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, for the purposes of this policy, are 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): An office within the U.S. Department of Health and Human Services (DHHS) responsible for providing leadership on human research participant protections and implementing a program of compliance oversight that provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research. OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research (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 an 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.

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 Specimen** – (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 swabs, 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.

PERSON OF INTEREST (POI): Type of UTRGV network account allowing for an unaffiliated individual's access.

PHARMACODYNAMICS (PD): The study of the molecular, biochemical and physiologic effects of administered substances. PD describes how biological processes in the body respond to or are impacted by the administered substances.

PHARMACOKINETICS (PK): The study of how the body interacts with administered substances for the entire duration of exposure. PK describes a drug's absorption, distribution, metabolism, and excretion properties.

PHASE I TRIALS: The first step in testing a new treatment in humans. A phase I clinical trial tests the safety, side effects, best dose, and timing of a new treatment. It may also test the best way to give a new treatment (for example, by mouth, infusion into a vein, or injection) and how the treatment affects the body. The dose is usually increased a little at a time in order to find the highest dose that does not cause harmful side effects. Phase I clinical trials usually include only a small number of patients who have not been helped by other treatments. Sometimes they include healthy volunteers. Also called phase 1 clinical trial.

PHASE II TRIALS: Phase II studies begin if Phase I studies do not reveal unacceptable toxicity. While the emphasis on phase I is safety, the emphasis in Phase II is 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 II studies ranges from a few dozen to about 300.

PHASE III: Phase III studies begin if evidence of effectiveness is shown in Phase II. 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 IV studies occur after a drug is approved. They may explore such areas as new uses or new populations, long-term effects, and how participants respond to different dosages.

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

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

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

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

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

PREPARATORY TO RESEARCH: Activities that include preparing a research protocol, developing a research hypothesis, and identifying prospective research participants.

PREVENTIVE ACTION: Action taken to eliminate the root cause of a problem or potential problem including the detection/identification of issues. See Corrective and Preventive 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: 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 was halted prematurely and will not resume).

PRINCIPAL INVESTIGATOR (PI): An individual who is responsible for conducting 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 the institutional research 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 monitors/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 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 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 standard for an individual's privacy rights, to enable them to understand and control how their health information is used. Within DHHS, the Office of Civil Rights (OCR) is authorized to implement and enforce the Privacy Rule.

PRIVATE INFORMATION: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order to be considered information to constitute research involving human participants.

PROSPECTIVE RESEARCH: 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): Information created or received by a UTRGV entity related to (a) the past, present, or future physical or mental health condition of a patient, or (b) payment for the provision of healthcare to a patient that is transmitted or maintained in any form or medium. PHI contains identifiers, such as demographic or 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 AMENDMENT: A written description of a change(s) to or formal clarification of a protocol.

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.

QUALIFIED PRESCRIBER FOR RESEARCH: A current state licensed prescriber who is able to prescribe drugs for humans in the state of Texas, 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 an Investigator or Co-Investigator.

QUALIFYING CLINICAL TRIAL/RESEARCH (QCT): A clinical research project that meets the requirements outlined in the Center for Medicare and Medicaid Services Clinical Trials Policy, which may qualify for reimbursement of routine costs from a third-party health insurance payer.

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 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.

QUERY: Any question raised during the review of a particular entry on a case report form which is open to different interpretations including various data errors. A query is a communication tool used in the clinical trial process to clarify or resolve any discrepancies or inconsistencies found in the data.

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 used.

RECORDS: Recorded information, regardless of medium or characteristic, which can be retrieved at any time. Records include 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. Draft or markups are not included (see below).

A. Entity business records include, but are not limited to, letterhead correspondence, legal options, 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 while 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 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., participants are being treated or examined), but enrollment has completed
- Completed: the study has concluded; participants are no longer being examined or treated (i.e., the last visit has occurred)
- Suspended: recruiting or enrolling activity has halted prematurely but potentially will resume

- Terminated: recruiting or enrolling activity 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 (Research Electronic Data Capture) is an open source, browser-based, metadata driven electronic data software and workflow methodology for designing clinical and translational research databases.

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.

REGULATORY BINDER: Compilation of essential regulatory documents related to a study. All studies conducted at UTRGV are required to keep a regulatory binder (paper or electronic). This is often the first collection of documents reviewed during audits and inspections.

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 REQUIREMENTS: Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products of the jurisdiction where the trial is conducted. (From FDA website)

REIMBURSEMENT: Refers to payment for expenses incurred by study participants such as parking, transportation, lodging, or meals while participating in clinical research. Reimbursement of 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 IRB 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". Common rule guidelines encourage the use of reliant review in any multi-site study.

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

RELYING IRB: "Relying IRB" refers to one or more IRB(s) deferring to another IRB for their oversight/services through a reliance agreement for a collaborative research project. One IRB can serve as the IRB of record, and any other IRBs relying on their services are the relying IRBs.

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. It does not include study medications or supplies that are necessary for the conduct of the study. Remuneration is considered taxable income to the research participant at $300 per year, per UTRGV policy.

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

RESEARCH INTEGRITY OFFICER: 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 related to participation in a clinical trial.

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, letters and emails necessary for reconstruction of study conduct that are generated and/or received while conducting the human research project.

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

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

ROUTINE COSTS: Items and services that are otherwise generally available to Medicare Beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision) that are provided in either the experimental of the control arms of a qualifying research project as defined by NCD 310.1.

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 judgement, 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 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 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.

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.

SINGLE-BLINDED STUDY: Study in which one party, either the investigator or participant, is unaware what medication the participant is taking.

SITE INITIATION VISIT (SIV): A meeting requested by the sponsor of a newly approved/activated trial for the study team at the clinical site to review the specifics of the protocol (e.g.: the science, design, procedures, CRF completion etc.) in preparation to enroll the first subject. It serves as initial training for all study staff present for their specific roles and responsibilities.

SITE QUALIFICATION VISIT: A meeting with the representative from a Sponsor to ensure the institution is fully capable of and equipped to run a specific clinical trial. This visit may also be referred to as Site Selection Visit (SSV) or Pre-Study Qualification Visit (PSQV). The Sponsor representative will usually request a tour of the facility and time to discuss the fundamentals of the protocol and how that relates to the feasibility of recruiting potential participants. Other topics include investigator responsibilities, qualifications of investigator and site personnel, study objectives, protocol required procedures, eligibility criteria, recruitment, IRB processes, informed consent requirements. adverse event reporting, source documentation, record retention, space requirements, drug/device storage, and availability of equipment.

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, subject diaries, evaluation checklists, pharmacy 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, lab, and at medical-technical departments involved in the research). 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 OPERATING PROCEDURES (SOP): Detailed written instructions to maintain standardization of a specific function.

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 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 PI at a trial site to perform clinical trial-related procedures and/or to make important trial-related decisions. ICH E6R2 1.56

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 or other trial related data.

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

SYSTEM ADMINISTRATOR (pertaining to Florence eBinders™): The role that is responsible for ensuring the appropriate training, education, experience, role assignment and access to users of the regulatory software.

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, that is being used as the object of investigation.

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 clinical trial site and associated costs such as mileage reimbursement, parking, transportation, meals, and lodging.

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

UNAFFILIATED ENTITY: An individual neither employed nor contracted by UTRGV, such as a monitor or auditor.

UNANTICIPATED PROBLEM INVOLVING RISKS TO SUBJECTS or OTHERS (UPIRHSO: The Office of Human Research Protections (OHRP) defines UPIRHSO as any event or outcome that was previously unforeseen and indicates that participants or others are at an increased risk of harm. OHRP considers unanticipated problems in general to include any incident, experience, or outcome that meet **all** of the following criteria:

1. Unexpected: not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application);
2. Related or possibly related to the participation in research (there is at least a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research; and
3. Increased risk of harm suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

UNDUE INFLUENCE: influence by which a person is induced to act otherwise than by their own free will or without adequate attention to the consequences. Unlike coercion, undue influence may be unintentional. For example, patient stipends in an economically disadvantaged patient population causing patients to consent to research treatments they would not otherwise consider.

UNEXPECTED ADVERSE EVENT: (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 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. An unanticipated event may be symptomatically and

pathophysiologically related to an event listed in the labeling but differs because of greater specificity or severity (21 CFR 56 Preamble).

UNIVERSAL PRECAUTIONS: Infection control measures used to reduce the risk of transmission of bloodborne pathogens through exposure to blood or bodily fluids. These preventative measures treat all blood and body fluids as infectious or disease carrying. Measures include:

- Single-use disposable injection or percutaneous equipment, or sterilized, if single-use equipment is not available.
- Discarding sharps, such as needles, scalpels, etc., without recapping, in rigid liquid-proof containers that are sealed and destroyed prior to being completely full.
- Washing hands with soap and water before and after procedures.
- Use of barriers such as gloves, gowns, goggles, or face mask to prevent contact with blood or body fluids.
- Disinfecting instruments and contaminated equipment and workspace.

VOLUNTARY: Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject's decision to participate in a research activity.

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 of 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 CONSENT: a state in which research activity and/or data collection is suspended or lost. The participant can withdraw their consent willingly when no longer wanting to participate in the research for any reason. An investigator can also withdraw a participant for ongoing non-compliance or if continuing the research would expose the participant to an unacceptable level of risk.