Human Research Protection Program at UT Southwestern

10.0 Glossary of Human Terms

Responsible Office: Human Research Protection Program Department (HRPPD)

Effective Date: September 3, 2026

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A

Accrual. The process of seeking eligible participants and obtaining their consent to participate in the research. Accrual generally starts with recruitment, leading to screening for eligibility, and consent to enroll in the study. *Also see Enrollment.*

Acknowledged. UT Southwestern Institutional Review Board (IRB) uses the term "*Acknowledged"* when a document or memo is sent to the IRB that does not, according to applicable regulations or policy, require IRB approval. In this way the Investigator and sponsor are administratively notified that the document or memo was received by the IRB and reviewed by the IRB staff to ensure any regulatory issues are addressed and placed in the protocol record.

Administrative Change. A modification to an approved IRB application which does not require IRB approval. Administrative changes should be submitted to IRB for review and acceptance.

Examples include (but are not limited to):

- Correction of typos
- Translations of approved consent forms and recruitment material,
- Verification of media advertisements based on IRB approved scripts,

- Minor changes to contact information,
- Removal of a study sites,
- Changes requested by affiliated institutions,

Changes that correct administrative errors made during previous IRB review.

Adverse Drug Experience/Reaction (ADR). The United States Food and Drug Administration (FDA) defines an ADR as any adverse event associated with the use of a drug in humans, whether or not considered drug related, including the following: an adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; or any failure of expected pharmacological action.

Adverse Event (AE). In general AE is used very broadly and encompasses physical and psychological harms and includes:

Any experience or abnormal finding that has taken place during the course of a research project and was harmful to the subject participating in the research, or increased the risks of harm from the research, or had an unfavorable impact on the risk/benefit ratio. The FDA also includes in its definition abnormal preclinical or laboratory findings which may not yet have resulted in direct harm to subjects (e.g., a bacteria is identified in a culture from the same batch of cells used to produce a vaccine which has been administered, even if no cases of infection have been reported). The event may or may not be caused by an intervention (e.g., headache following spinal tap, death from the underlying disease, car collision).
Adverse Events can include psychological, social, emotional, and financial harms. 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 it is considered related to the subject's participation in the research. See also, Serious Adverse Event.

Advocate. An individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the clinical investigation.

Affiliated Institution. Is any institution that relies on UT Southwestern's IRB.

A signed agreement between the relying institution and the IRB is required to establish the affiliation. There are three general categories of institutional agreements: 1) a **blanket agreement** indicates that any study from the relying institution can be reviewed by the IRB (e.g., Southwestern Health System) 2) a **limited agreement** applies to a defined category or group of studies (more than one study) and 3) a **single study** agreement applies to a single-study. Single-study agreements may be covered under an Investigator Authorization Agreement (IAA) without a Memorandum of Understanding or Agreement (MOU/MOA). However, blanket and limited agreements generally require both an IAA and an MOU/MOA.

Agent. Used to indicate when an individual is working on behalf of the institution (i.e., performing UT Southwestern designated activities or exercising UT Southwestern delegated authority or responsibility) in relation to research. An agent can be an employee of the institution (e.g., faculty or staff) or a non- employee who is authorized by the institution to act on behalf of the institution (e.g., student, affiliated faculty, emeritus professors).

An institution is considered Engaged In Research_Individuals when an Employee or agent of the institution conducts human research activities.

It is possible for a UT Southwestern employee to conduct research and not be considered an agent of the university if the research is conducted during non-official duty time, is not in connection with her/his UT Southwestern responsibilities, is not being conducted at a UT Southwestern facility and the research is not supported by a direct UT Southwestern award to the UT Southwestern (review the Handbook of Operating Procedures (HOP) on Conflict of Commitment). The institution however generally reserves the right to determine for themselves whether their employee (in whole or in part) is performing institutionally designated activities and acting on behalf of the institution or exercising institutional authority or responsibility in regard to that research and the IRB will generally consider this in determining whether the institution in question is engaged in research.

Allegation of noncompliance. An unconfirmed report of noncompliance.

Alternate member. An individual appointed to the IRB to serve in the same capacity as the specific IRB member(s) for whom the alternate is named, who substitutes for the member at convened meetings when the member is not in attendance. *Note: IRB members and alternates have equal responsibilities in terms of required education, service, and participation.*

Amendment. Any changes to previously approved research. Investigators may not initiate any changes in research procedures or consent form(s) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject (Note: IRB approval of the actions taken in this circumstance must still be sought after the fact). See also Major Change Or Modification

Anonymous. Anonymous means entirely without name or identifier, so the individual cannot be discerned in any way by anyone. No one can link an individual person to the responses of that person, including the investigator. For this reason, face-to-face interviews are never anonymous. If phone numbers are not stored, then telephone

interviews could be considered anonymous. Questionnaires that are returned via US Mail are considered anonymous only if no tracking codes are used.

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

Appropriate Institutional Officials. Officials determined by each organization to be points of contact for research. This may include an individual, an office or a committee. (This term should not be confused with another similar but distinctly different DHHS term Authorized Institutional Official).

Approval Date. The first date that research can be performed (following notification from the IRB), consistent with federal regulations, state and local laws, and university policy. The approval date is the date that the research is approved by convened or expedited review, or if modifications are required (to secure approval), the date that modifications/conditions are met by the investigator.

Approval Period. For initial review, the interval that begins on the day research is approved by convened or expedited review, or if modifications are required (to secure approval), the date that modifications/conditions are met by the investigator. For continuing review, the interval that begins on the day research is re-approved (by convened or expedited review) or modifications are required. *Note: An approval period for initial or continuing review may not be longer than one year*.

Approved. An IRB action taken when the required determinations are made that allow research involving human subjects to proceed consistent with federal regulations, state and local laws, and university policy.

Assent. Affirmative agreement by an individual not Competence to give legally valid

informed consent (e.g., child or person with limited mental capacity) to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Association for the Accreditation of Human Research Protection Programs (AAHRPP). The AAHRPP promotes high quality research through an accreditation process that helps organizations worldwide strengthen their human research protection programs. An independent, non-profit accrediting body, AAHRPP uses a voluntary, peer-driven, educational model to ensure that HRPPs meet rigorous standards for quality and protection. To earn accreditation, organizations must provide tangible evidence, through policies, procedures, and practices, of their commitment to scientifically and ethically sound research and to continuous improvement.

Assurance Of Compliance. An assurance of compliance is a written document submitted by an institution (not an Institutional Review Board) that is Engaged In Research with Individuals in non-exempt human subjects research conducted or supported by a specific federal agency. Through the assurance, an institution commits to the governing agency that it will comply with the requirements set forth in the regulations for the protection of human subjects. For research supported or funded by DHHS, the Federalwide Assurance is the only type of assurance accepted and approved by UT Southwestern's Office of Human Protections Program (HRPP).

Assured Institution. An institution holding an approved assurance from the applicable federal agency.

Authorization. As outlined in 45 CFR 160 and 164 (HIPAA): An individual's written permission to allow a covered entity to use or disclose specified PHI for a particular purpose.

Authorized Institutional Official. Within the institution, there must be a point of responsibility for the oversight of research and IRB functions. This point should be an

official of the institution who has the legal authority to act and speak for the institution, and should be someone who can ensure that the institution will effectively fulfill its research oversight function. The authority can be delegated.

Authorized Representatives. HIPAA 45 CFR - 164.502(g) defines authorized personal representatives as persons who have the authority under applicable law to make health care decisions on behalf of adults or emancipated minors, as well as parents, guardians or other persons acting in loco parentis who have the authority under applicable law to make health care decisions on behalf of unemancipated minors.

Persons who are authorized under Texas state law to make health care decisions on behalf of other individuals will also be personal representatives under HIPAA.

Audit. A systematic review, inspection, or verification, typically conducted by an independent individual or group.

Autonomy. Personal capacity to consider alternatives makes choices, and act without undue influence or interference of others.

Advocate (Ward of the State. For research involving children who are wards of the state or another institution, the IRB must appoint an advocate for each child when required by applicable regulations. The advocate serves in addition to any guardian or individual acting in loco parentis and has the background and experience necessary to act in, and agrees to act in, the best interests of the child. The advocate must not be associated in any way, other than in the role of advocate or IRB member, with the research, the investigators, the guardian, or the organization responsible for the child's care.

B

Bank (Tissue). Collection of data and/or specimens obtained and stored for future

research uses and/or distribution, including a collection not originally or primarily obtained for research purposes.

Behavioral Research. The scope and diversity of research areas in the behavioral and social sciences is quite broad. Some research is readily applicable to human affairs; other studies may broaden understanding without any apparent or immediate application. Some research is designed to test hypotheses derived from theory; other research is primarily descriptive. Still other research may be directed at evaluating an intervention or social program. Behavioral research involving human subjects generates data by means of questionnaires, observation, studies of existing records, and experimental designs involving exposure to some type of stimulus or intervention.

Belmont Report. Ethical Principles and Guidelines for the protection of human subjects of research. On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research, and (iv) the nature and definition of informed consent in various research settings.

Beneficence. Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. Two general rules have been formulated as expressions of beneficent actions (Belmont Report, 1978):

1. Do no harm, and
2. Maximize possible benefits and minimize possible harms

Benefit. Something that promotes or protects well-being; an advantage. Compensation cannot be considered a benefit. Just as there are a range of harms: physical, social, economic, psychological, and legal, there can also be a range of benefits: physical benefit is clinically beneficial - as with standard-of- care procedures known to be helpful in guiding the subject's care when plans include using them as such (experimental procedures or procedures that must be verified by an approved device might not result in this benefit), notwithstanding that the subjects could have received the benefit without being in the study (this information comes to light in the alternatives description); psychological benefit of educational, informational, counseling or other resources provided in the study or empowerment. These can be directed at the individual (direct benefit, secondary benefit, monitoring benefit), the community or a general knowledge gained benefit (philanthropic on behalf of the individual). Only certain anticipated benefits may be considered appropriate for consideration to weigh against the probability of harm in certain populations and circumstances.

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

Biography or Oral History. Interviews that collect, preserve and interpret the voices and memories of people, communities, and participants in past events as a method of historical documentation. The intent is to document a particular past or unique event in history.

Biological product. A biological product (biologic) is a medical product. Many biologics are made from a variety of natural sources, such as humans, animals or microorganisms. Like drugs, some biologics are intended to treat diseases and medical

conditions. Other biologics are used to prevent or diagnose diseases. Examples of biological products include:

- Vaccines
- Blood and blood products for transfusion and or manufacturing into other products
- Allergenic extracts, which are used for both diagnosis and treatment, such as allergy shots
- Human cells and tissues used for transplantation, such as tendons, ligaments and bone
- Gene therapies
- Cellular therapies
- Tests to screen potential blood donors for infectious agents, such as HIV
- In general, the term "drugs" includes therapeutic biological products

Blind. A randomized study is "Blind" if the participant is not told which arm of the study he is on. A clinical project is "Blind" if participants are unaware on whether they are in the experimental or control arm of the study; also called masked.

Blinded Study Design. A study in which one party, either the investigator or participant, is unaware of what medication or study arm the participant is assigned to (Single-Blind study). A clinical study design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo or another therapy (Double-Blind study). Double- blind studies are thought to produce more objective results, since the impact of expectations of the doctor and the participant about the experimental drug are minimized. Also referred to as a "masked" study.

Bonus Payment. Compensation tied to the rate or timing of recruitment or performance or other aspects of a clinical study. Examples of bonus payments include the following:

- the sponsor announces that the highest enrolling site in the nation will receive a $10,000 bonus;
- the sponsor offers to pay an additional $10,000 beyond the budgeted study costs to any site that enrolls five participants within a week;
- the sponsor offers to pay an additional $10,000 beyond the budgeted study costs to any site that fulfills its recruitment target by the end of the month; the sponsor offers to pay an additional $1,000 beyond the budgeted study costs for any subject who agrees to enroll within one day of initial contact.
  This does not include compensation for services rendered which include screening and referral activity unrelated to whether the participant ultimately enrolls in or completes the research study.

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Capacity. The ability based on reasonable medical judgment to understand and appreciate the nature and consequences of a treatment decision, including the significant benefits and harms of and reasonable alternatives to any proposed treatment decisions. Subjects who are incapacitated are not capable of giving informed consent for research but may be capable of providing assent. Also see Incapacitated and Impaired Decision-Making Capacity.

Case Report Form (CRF). A paper or electronic questionnaire specifically used in clinical trial research. The CRF is the tool used by the sponsor of the clinical trial to collect data from each participating site. All data on each patient participating in a clinical trial are held and/or documented in the CRF, including adverse events. Information captured in a CRF must be supported by a Source Document (unless the CRF is the source document).

Example Source Documents

Original Study Documents – Completed Informed Consent Forms (ICF) and Case Report Forms (CRF) Records from study execution or supporting documents on medical history including the following:

- Medical records
- Hospital, clinic, & office charts
- Progress notes, patient visit notes, physician's notes/orders
- Records: laboratory, radiology, cardiology, medico-technical departments
- Pharmacy dispensing records
- X-Rays, Scans (bone, brain, MRI)
- Video (angiography, endoscopy)
- Instrumentation print-out: EKG, ECG, Spirometry, etc.
- Memos to record concerning the study
- Subjects' diaries, evaluation checklists, or Quality of Life questionnaires
- Recorded data from automated instruments
- Certified transcription of recorded results including dictation (i.e., verified as accurate and complete)
- Photographs, negatives, microfilm or magnetic media

Cause. An assessment made by the investigator and/or sponsor regarding the proper attribution of an adverse event. Examples: Study intervention (e.g., drug, device, or therapy); Concurrent non-research therapy; Disease progression; Other or unknown source.

Certificate of Confidentiality. A Certificate of Confidentiality helps researchers protect the privacy of human research participants enrolled in biomedical, behavioral, clinical and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identifying characteristics of a research participant. Researchers may apply for a Certificate through

the NIH or Center funding the research, Contact information is available on the NIH website at: http://grants2.nih.gov/grants/policy/coc/index.htm

Certification. The official notification by the institution to the DHHS that a research project or activity involving human subjects has been reviewed and approved by the IRB in accordance with the approved assurance on file at DHHS. In order for a proposal involving human subjects to be eligible for federal funding, it must first be approved by the IRB and certified by the institutional representative.

Certified Translation. A certified translation is one that has been formally verified by a licensed translator or translation company for use in official purposes. Certified translators attest that the target- language text is an accurate and complete translation of the source-language text. Certified translation of consent documents ensures that the tone, meaning and content of the translated documents remain consistent with the IRB-approved English version.

Child/Children. Person(s) who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. For purposes of HRPP policy, individuals under 18 years of age are considered children in Texas unless they meet the definition of emancipated minors. *See* Minor.

Class Project. Academic projects or student assignments involving collection of data from human subjects, when the data is used solely for the purpose of teaching course content and not intended to be used to develop or contribute to generalizable knowledge.

Classified Research. In the interest of national security, federally funded research can be 'classified' in terms of limited access to data, information, and facilities (inputs) that may be required to carry out the research or in terms of the limited distribution of the

results of the research (outputs).

Interested parties should contact the involved institution's Security Officer for further information regarding security clearances, classified document control, foreign visitor information, security inspections, and so forth.

Clinical Equipoise. A genuine uncertainty on the part of the expert medical community about the comparative therapeutic merits of each arm of a clinical trial. When the relative benefits and risks of the proposed intervention, as compared to standard therapy, are unknown, or thought to be equivalent or better, there is clinical equipoise between the historic intervention and the proposed test intervention.

Clinical Investigation. Involves the use of a Test Article (i.e., drug, device, food substance or biologic) and one or more human subjects. This applies to test articles that require prior submission to the FDA and those that do not if the results of the investigation are intended to be part of an application to the FDA for a research or marketing permit. It does not include the use of FDA approved devices or drugs in routine medical practice. (21 CFR 50.3(c), 21 CFR 56.102(c)) *Note: Non-clinical laboratory studies are not considered to be clinical investigations. See the DHHS definition of research for DHHS-regulated research.*

Clinical Trial. *Pre-2018 Common Rule Definition:* Any investigation in human subjects intended to: discover or verify clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product; identify any adverse reactions to an investigational product; and/or study absorption, distribution, metabolism, and excretion of an investigational product to determine its safety and/or efficacy. *Note: Studies involving only behavioral interventions are not covered by this policy.*

2018 Common Rule Definition: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or

other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Clintrials.gov. A registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

Co-Principal Investigator. The Local PI may designate a Co-Principal Investigator (Co-PI) to assist with local PI responsibilities (e.g., report unanticipated problems, authorize modifications or progress reports). The primary authority and accountability for the conduct of the research may not be assigned or delegated to the Co-PI although they are considered to share equal responsibility for all aspects of the study and are both allowed to submit any IRB required reports/requests.

Code of Federal Regulations (CFR). The CFR is a codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government. The CFR is divided into 50 titles representing broad areas subject to Federal Regulation. Each Title is divided into chapters that are assigned to agencies issuing regulations pertaining to that broad subject area. Each chapter is divided into parts and each part is then divided into sections -- the basic unit of the CFR. The purpose of the CFR is to present the official and complete text of agency regulations in one organized publication and to provide a comprehensive and convenient reference for all those who may need to know the text of general and permanent Federal regulations.

45 CFR 46: The Federal Policy for the Protection of Human Subjects published in 1991. It includes 4 subparts:

- Subpart A- also known as the “Common Rule,” the basic Health & Human Services policy for protection of Human Research Subjects.
- Subpart B - additional protections for pregnant women, human fetuses,

and neonates involved in research.

- Subpart C - additional protections involving prisoners as subjects.
- Subpart D - additional protections for children involved as subjects in research.

21 CFR: Title 21 of the Code of Federal Regulations (CFR) pertains to the rules of the Food and Drug Administration (FDA). Each title (or volume) of the CFR is revised once each calendar year. It includes multiple parts; the most commonly referenced in clinical research being:

- 21 CFR 11- (also known as part 11) sets forth the criteria under which the agency (FDA) considers electronic records, electronic signatures, and handwritten signatures to be trustworthy, reliable, and generally equivalent to paper records and handwritten signatures executed on paper.
- 21 CFR 50- applies to all clinical investigations regulated by the FDA under sections 505(i) and 520(g) of the act, as well as clinical investigations that support applications for research and marketing permits for products regulated by the FDA including foods, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, and electronic products. Note: This section also includes a subpart D with similar protections for children.
- 21 CFR 56- outlines the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinical investigations regulated by the FDA under sections 505(i) and 520(g) of the act, as well as clinical investigations that support applications for research and marketing permits for products regulated by the FDA including foods, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, and electronic products.
- 21 CFR 312- contains procedures and requirements governing the use of investigational new drugs, including procedures and requirements for the

submission to, and review by, the Food and Drug Administration of investigational new drug applications (IND's).

- 21 CFR 314- sets forth procedures and requirements for the submission to, and the review by, the Food and Drug Administration of applications and abbreviated applications to market a new drug under section 505 of the Federal Food, Drug, and Cosmetic Act, as well as amendments, supplements, and post-marketing reports to them.
- 21 CFR 812- provides procedures for the conduct of clinical investigations of devices. An approved investigational device exemption (IDE) permits a device that would otherwise be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the pu pose of conducting investigations of that device.
- 21 CFR 814- implements sections 515 and 515A of the act [Federal Food, Drug, and Cosmetic Act] by providing procedures for the premarket approval of medical devices intended for human use.

Coded information and data. (1) Identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Coded pre-existing or coded prospective data or specimens. if 1) the private information/specimens were not/will not be collected specifically for the currently proposed research through an interaction or intervention with living individuals, or 2) the investigator(s) never obtains identifiable data/specimens because: a) the holder of the key to decipher the code, destroys the key before the data is provided to the investigator, or b) the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, or until the individuals are deceased; or there are laws or IRB-approved written policies for a repository/data management center that prohibit the release of the key to the investigators under

any circumstances, until the individuals are deceased.

Coercion. This occurs when an overt threat of harm is intentionally presented by one person in order to obtain compliance (Belmont Report). To be coercive, a subject who refuses must be made worse off than if he or she would have been, if never asked even if the harm is only perceived. Coercion occurs, for example, in cases where retribution is conceivable or perceived by the subject. Examples of coercion include situations where it is implied that continued services are dependent upon participation in the research; or where refusal may affect some future care or outcome. Inducements (including payment) are not considered coercion for the purposes of UT Southwestern HRPP applications of policy. *See* Undue Influence *concerning when judgment may be compromised by financial incentives especially when the subject is not the recipient of the financial incentive)*.

The HRPP must eliminate all sources of coercion.

Cognitively Impaired. While having either a psychiatric disorder (e.g., psychosis, neurosis, personality, or behavior disorder), a developmental disorder (e.g., mental retardation), or a neurological disorder that affects cognitive or emotional functions to the extent that capacity for judgment is significantly diminished may be considered to have a Diminished Autonomous Decision-Making Capacity (DADMC), cognitively impaired should not be automatically considered to be unable to provide valid consent or assent. Additionally, other individuals may also be considered by the PI or the IRB to be cognitively- impaired or have a Diminished Autonomous Decision-Making Capacity (DADMC) or have limited decision- making ability because they are under the influence of drugs or alcohol, suffering from degenerative diseases affecting the brain, are terminally ill, or have disabling physical handicaps, depending on the circumstances.*(Also see Mentally Disabled, Diminished Autonomous Decision-Making Capacity (DADMC), Handicapped)*

Cohort. A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.

Cohort Study. A form of longitudinal study used in medicine and social science.

Collaborating Individual Investigator. This term is limited to collaborative research between an institution with a Federalwide Assurance and an outside researcher. The local implementation of these type agreements is as follows. The research covered by this agreement must be conducted under the direction and supervision of a UT Southwestern Principal Investigator or a PI from an UT Southwestern Affiliated institution. The collaborating individual investigator may not be an employee or agent of a UT Southwestern Affiliated Institution and must be conducting the collaborative research activities outside the facilities of the affiliated institution(s). There are two types of collaborating individual investigators:

1. A collaborating **independent** investigator is not acting as an employee of **any** institution with respect to his or her involvement in the research being conducted by the assured institution(s).
2. A collaborating **institutional** investigator is acting as an employee or agent of a non-assured institution with respect to his or her involvement in the research being conducted by the assured institution and the non-assured institution that does not routinely conduct human subjects research.

Collector Of Data/Specimens. Anyone who obtains data/specimens from the source and provides it to the Management Center/Repository, see Repository, for storage. A collector (sometimes referred to as collector-investigator) can be from an organization covered by the UT Southwestern IRB or from an organization not covered by the UT Southwestern IRB. The source is where the data/specimens originated (e.g., hospital pathology department, electronic record system, or a research study).

Community-Based Participatory Research. A collaborative research approach that is designed to ensure and establish structures for participation by communities affected by the issue being studied, representatives of organizations, and researchers in all aspects of the research process to improve health and well-being through taking action, including social change (Agency for Healthcare Research and Quality- AHRQ)

Common Rule. The 'Common Rule' is the Federal Policy for the Protection of Human Subjects, as set forth in 45 CFR 46 subpart A, and parallel regulations promulgated by agencies such as the FDA.

Compassionate Use (Expanded Access). While the phrase "compassionate use" is commonly used to describe some of the ways of making unapproved products available to patients, the technical term for this is Expanded Access (to investigational drugs or devices for treatment). The use of an investigational drug or device when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition. The distinction between expanded access and the use of an investigational drug (or device) in the usual studies covered under an IND (IDE) is that expanded access uses are not primarily intended to obtain information about the safety or effectiveness of a test article. Although not considered research, the FDA requires IRB approval prior to non-emergency use. (IRB approval required).

Compensation. Compensation is payment for participation in research and should be the same for each subject as opposed to Reimbursement which may be different for each subject if for example reimbursement is based on verification of travel expenses, etc. *Note: Compensation could also be considered payment or medical care for study-related injury in certain circumstances.*

Compensation For Services Rendered. Compensation for recruitment and screening related activities that are unrelated to whether the participant ultimately enrolls in or completes the research study (such as advertising, administrative and personnel costs)

or compensation for the costs of services provided to those individuals who do ultimately enroll. Investigators should be sure to determine a reasonable budget amount that is directly related to the value of the services provided to the study, and to document how that amount was determined.

Examples include the following:

- the budget might include a portion of the salary of individuals that is related to the time spent recruiting and screening potential research participants (regardless of whether they are successful in recruiting those participants),
- time spent for subsequent study visits,
- survey administration, and so forth.

Staff may not be paid a fee for every successful recruitment (e.g., $10 for every participant who signs the consent document to participate in the study). Further, any payments to University for personnel must be reflected in the study budget and in the written agreement that is reviewed by Sponsored Programs Administration (SPA).

Competence. Technically a legal term, used to denote Capacity to act in 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.

(Also see Mentally Disabled, Diminished Autonomous Decision-Making Capacity (DADMC), Handicapped, Incompetent, Capacity)

Competitive Enrollment. Indicates that the local site may enroll more subjects than originally planned by the study sponsor. In this situation, the total number of subjects enrolled study-wide does not change.

Compliance. In relation to research: Adherence to all relevant trial-related requirements, good clinical practice (GCP) requirements, and the applicable

institutional, state and federal regulatory requirements.

Concurrent Control. A concurrent or prospective control is a subject who is not given the treatment or intervention under the study and who is compared with subjects given the treatment under the study. There are **three types** of concurrent controls: a concurrent control may be given a placebo (concurrent placebo control) or no treatment (a non-treatment concurrent control), or an active drug (a concurrent active control).

Confidential Disclosure Agreement (CDA). Sometimes called a 'Confidentiality Agreement' or 'Non- Disclosure Agreement', is a legal document which ensures the confidentiality or 'secrecy' of information that one party discloses to another party.

Confidentiality. In the context of human subjects research, the condition that results when data are maintained in a way that prevents inadvertent or inappropriate disclosure of participants' identifiable information.

Conflict of Interest. Any interest that could reasonably be expected to affect the objectivity of an IRB member or consultant in relation to an application or other matter under IRB review. An IRB member or consultant has a conflict of interest if the individual:

- Is or will be an investigator or member of the research team (that is, listed on the IRB application)
- Is Has an immediate family member (that is, spouse, dependent children) or personal relationship with an individual who is one of the investigators
- Has a financial or managerial interest in a sponsoring entity or product being evaluated or provided by a commercial entity in the research, as defined by UT Southwestern Conflict of Interest Policy

- Has received or will receive compensation with value (as defined by UT Southwestern Conflict of Interest Policy) that may be affected by the outcome of the research project

- Has a proprietary interest in the research, such as a nonprovisional patent application, patent, trademark, copyright or licensing agreement as defined by UT Southwestern Conflict of Interest Policy
- Has a nonfinancial interest (personal circumstance, ethical belief, or other factor) that may be conflicting, for example, the IRB member has an interest that he or she believes conflicts with his or her ability to review a project objectively

Consent. Consent is a person's voluntary agreement to participate in research or to undergo a diagnostic therapeutic or preventive procedure in contrast to the term Informed Consent which is making this decision with a knowledge and understanding of the relevant information and Legally Effective Informed Consent of the subject or the subject's legally authorized representative as outlined in 45 CFR 46 (Common Rule). *Also see Mentally Disabled, Diminished Autonomous Decision-Making Capacity (DADMC), and Handicapped. Also Informed Consent or Legally Effective Informed Consent.*

Consent document. A structured, written description in understandable terms of relevant research project information. The consent document is not consent itself; it is the record of what has been communicated to a potential participant. It is the document that ensures all regulatory elements are present and communicated to a potential participant. When signed by the potential participant, the consent document is a record of the receipt of research-related information by the participant. It also serves as reference material for the participant as the research project progresses. It is not a contract and is not legally binding, and the participant may choose to withdraw consent at any time.

Consortium Agreement. Group of collaborative investigators/institutions; an arrangement that can be formalized with specified terms and conditions.

Consultant. A scientist or nonscientist from within or external to UT Southwestern who has special expertise to act — at the request of the IRB — as an ad hoc reviewer of a research project application. These individuals have access to all documents relevant to the specific project under review, may participate in the deliberations and make recommendations on the project, but may not vote and are not counted toward quorum.

Continuing noncompliance. A pattern of repeated noncompliance (in one or more protocols simultaneously or over a period of time) which continues **after** initial discovery, including inadequate

efforts to take or implement corrective or preventive actions within a reasonable timeframe, which may or may not also constitute Serious Noncompliance.

Continuing Review of Research. Designates the review of requests to re-approve a study for continuation at any time after initial approval is granted. Periodic review of research activities at intervals appropriate to the degree of risk, but not less than once per year. The criteria for approval are defined by federal regulations.

Contract Research Organization (CRO): An independent contractor with the sponsor who assumes one or more of the obligations of the sponsor.

Controlled Study. Before a new drug or biologic can be marketed, its sponsor must show, through adequate and well-controlled clinical studies, that it is effective. A well-controlled study permits a comparison of subjects treated with the new agent with a suitable control population, so that the effect of the new agent can be determined and distinguished from other influences, such as spontaneous change, "placebo" effects, concomitant therapy, or observer expectations. FDA regulation 21 CFR 314.126 cites five different kinds of controls that can be useful in particular circumstances:

1. placebo concurrent control
2. dose-comparison concurrent control
3. No-Treatment Control, also No-Treatment Concurrent Control.
4. active-treatment concurrent control, and
5. historical control

No general preference is expressed by the FDA for any one type, but the study design chosen must be adequate to the task.

Convened IRB Review: Review of proposed human subjects research by an

Institutional Review Board that meets the membership requirements specified in federal regulations regarding the number, qualifications, diversity, and affiliation of its members, at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas.

Cooperative Agreement. An award similar to a grant, but in which the sponsor's staff may be actively involved in proposal preparation, and anticipates having substantial involvement in research activities once the award has been made.

Cooperative Research. In cooperative research, UT Southwestern investigators (employees/agents) are engaged in research or UT Southwestern will receive a direct federal (DHHS) award to conduct human subjects research, even where all activities involving human subjects are carried out by a non-UTSW entity (e.g., subcontractor or collaborator).

The UT Southwestern PI may be: 1) the Lead PI for the entire collaborative study (e.g., coordinates or directs the research at all study locations), 2) a collaborating investigator under the direction of a Lead PI from another institution, or 3) a collaborating investigator equally sharing the Lead PI responsibility with a local PI.

The Off-Site Research study site may be either: 1) an institution that regularly relies on the IRB for review and continuing oversight of research Affiliated Institution, or 2) an institution that is not normally affiliated with the IRB. The employees of an off-site location that is part of the cooperative research may or may not be Engaged In Research Individuals. An off-site institution or facility may be domestic or international and may or may not have its own IRB. *Also see* Off-Site Research.

Covered Entity. ***Federal****:* Health plans, health care clearinghouses and health care providers who transmit any health information in electronic form in connection with a transaction that is subject to federal HIPAA requirements, as those terms are defined

and used in the HIPAA regulations 45 CFR Parts 160 and 164. ***Texas State****:* Texas Health and Safety Code, Chapter 181, Medical Records Privacy: (2) "Covered entity" means any person who: (A) for commercial, financial, or professional gain, monetary fees, or dues, or on a cooperative, nonprofit, or pro bono basis, engages, in whole or in part, and with real or constructive knowledge, in the practice of assembling, collecting, analyzing, using, evaluating, storing, or transmitting protected health information. The term includes a business associate, health care payer, governmental unit, information or computer management entity, school, health researcher, health care facility, clinic, health care provider, or person who maintains an Internet site; (B) comes into possession of PHI: Protected Health Information; (C) obtains or stores protected health information under this chapter; or (D) is an Employee, Agent, or contractor of a person described by Paragraph (A), (B), or (C) insofar as the employee, agent, or contractor creates, receives, obtains, maintains, uses, or transmits PHI: Protected Health Information.

Therefore, in Texas, all healthcare providers must comply with the provisions relating to notice of privacy practices and access, amendment and uses and disclosures of protected health information, even if they do not engage in electronic transactions

Custom Device. A custom device means a device that:

(1) Necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician or dentist;

(2) Is not generally available to, or generally used by, other physicians or dentists;

(3) Is not generally available in finished form for purchase or for dispensing upon prescription;

(4) Is not offered for commercial distribution through labeling or advertising; and

(5) Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

A custom device may be exempt from the requirement for prior submission to the FDA for an IDE unless the device is being used to determine safety or effectiveness for commercial distribution. Note in some cases where not exempt, a custom device may still qualify for abbreviated requirements, in which case prior submission to the FDA for an IDE may not be required prior to IRB approval.

Customer Satisfaction Survey. This refers to surveys of program users to obtain feedback for use by program managers. This is similar to program evaluation.

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Data. When data is anonymous, they are not linked to the identity of individual subjects in any way that would make it possible to connect the information to the individual from whom it came. Anonymous data does NOT have direct identifiers like names, addresses, clinic or hospital number, Social Security Number, or insurance agency numbers. Data that is linked to subjects via a CODE are NOT anonymous. When data is confidential, there is a link between data and the individuals who provide it, but the link is obscured by coding or other procedures so that even someone who has access to the raw data cannot identify a subject without also having access to the link between the subject code and the subject's identity.

Data Management Centers. Facilities that collect, store, and distribute human data for research purposes. Data management activities involve three components: (1) the collectors of data; (2) the data storage and management center; and (3) the recipient investigators. Data management centers may be combined with human Repository.

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

Data and safety monitoring board (DSMB). A data safety monitoring board is an independent committee set up specifically to monitor data throughout the duration of a study to determine if continuation of the study is appropriate scientifically and ethically. Factors that suggest a DSMB is needed:

- A large study population and
- Multiple study sites. It is more difficult to recognize a pattern of increased or unusual problems or events when investigators treat small fractions of the population separately;
- Highly toxic therapies or dangerous procedures;
- High expected rates of morbidity or mortality in the study population;
- High chance of early termination of the study. DSMB membership is usually comprised of experts in the fields of medicine and science that are applicable to the study — statistical experts, lay representatives and others who can offer an unbiased assessment of the study progress.

Data and safety monitoring plan (DSMP). A data and safety monitoring plan (DSMP) is meant to ensure that each clinical investigation has a system for appropriate oversight and monitoring of the conduct of the clinical investigation. The purpose of a DSMP is to

ensure the safety of the participants, the validity of the data and the integrity of the study, and the appropriate termination of studies for which significant

benefits or risk has been uncovered or when it appears that the investigation cannot be concluded successfully. A DSMP is commensurate with the risks involved with the research study. The DSMP may include a data and safety monitoring board (DSMB).

Data use agreement. An agreement into which UT Southwestern and the investigator enter with the intended recipient of a limited data set that establishes the ways in which the information in the limited data set may be used and how it will be protected.

Debriefing. Giving subjects previously undisclosed information about the research project following completion of their participation in the Research**.**

Deception. The intentional misleading of subjects or the withholding of full information about the nature of the experiment. Misleading or omitted information might include the purpose of the research, the role of the researcher, or what procedures in the study are actually experimental. Deception increases ethical concerns, because it interferes with the ability of the subject to give informed consent. However, deception is arguably necessary for certain types of behavioral research. Because humans act differently depending on circumstances, full knowledge by the subject might bias the results.

Some research can only be conducted without the full knowledge of the research subjects. Yet the use of deception in research raises special problems that the IRB will review closely. One consideration is whether the deception is necessary. Present federal rules prohibit the use of deceptive techniques which place subjects at more than minimal risk.

Debriefing - IRBs expect investigators to debrief subjects who have been deceived during participation in research activities. The debriefing should include a detailed description of the ways in which deception was used. The investigator is responsible for ensuring that the subject leaves the research setting with an accurate understanding of

the deception. The debriefing process, including any written materials, should be explained to the IRB as a part of submitted protocols.

Declaration of Helsinki. An international ethical code first issued in 1964 by the 18th World Medical Assembly in Helsinki, Finland. The Declaration contains 12 basic principles, which are similar to the Nuremberg Code, but represent an expansion of what constitutes acceptable Research and the ethical responsibilities of investigators. Unlike the Nuremberg Code, the Declaration of Helsinki addresses the need for peer review (i.e., IRB review). It is interesting to note that the FDA will not accept foreign data unless the studies in which such data are generated are conducted in compliance with the Declaration of Helsinki (21 CFR 312.20, 46 Fed Reg 8953; Tuesday, January 17, 1981).

Belmont Report: A report consisting of ethical principles and guidelines for protection of human subjects in Research. It was issued April 18, 1979, by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

Deferred. An IRB action taken when the IRB cannot fully evaluate the research under review and make the determinations required for approval without modifications to the protocol and/or informed consent document, or submission of clarifications or additional materials prior to reconsideration of the research. *Note: Convened IRB review of the investigator's response(s) is required.*

De-identified health information. All direct personal identifiers are *permanently* removed (e.g., from data or specimens), no code or key exists to link the information or materials to their original source(s), and the remaining information cannot reasonably be used by anyone to identify the source(s). *Note: For purposes of HRPP policy, health information is de-identified when it does not contain any of the 18 identifiers specified by the HIPAA Privacy Rule at 45 CFR Part 164 (or has been determined to be de-identified by a statistician in accordance with the standards established by the Privacy Rule).*

The 18 identifiers:

1. Names
2. All geographical subdivisions smaller than a state, including street address, city, county, precinct, ZIP code and their equivalent geocodes, except for the initial three digits of a ZIP code, if according to the current, publicly available data from the U.S. Census Bureau:
    1. The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people, and
    2. The initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people are changed to 000;
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Phone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social Security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate and license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;
14. Web Uniform Resource Locators (URLs);
15. Internet Protocol (IP) address numbers;
16. Biometric identifiers, including finger and voice prints;

17. Full-face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic or code (note this does not mean the unique code assigned by the investigator to code the data).

Department or Agency Head. If an institution engaged in research is subject to an assurance to said department or agency, federal reporting requirements include reports to said department or agency heads. Reports are made generally to OHRP when the department is DHHS, but if not DHHS, then reports shall also be made to OHRP in addition to said department or agency head.

(See Department or Agency Heads, http://www.usa.gov/directory/federal/index.shtml)

Designated Reviewer. One or more experienced reviewers designated by the Chair from among the members of the IRB. Experience is determined by review of CV and interview with IRB Chair or HRPP Director and includes previous experience on IRBs (or other research review committees), or research regulatory/ethical education.

Deviation. Minor or administrative changes from the approved study protocol without prior IRB approval that are generally noted or recognized after it occurs, or if identified before it occurs, cannot be prevented by the investigator (not an intentional deviation). Deviations have no potential substantive effect on the risks to research participants or the scientific integrity of the research plan or the value of the data collected. Deviations are limited to minor departures from the protocol for a single subject and do not result from willful or knowing misconduct on the part of the investigator(s).

Device. A device per the FDA is: "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: 1) recognized in the United States Pharmacopeia–National Formulary (USP–NF), or any supplement to them, 2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation,

treatment, or prevention of disease, in man or other animals, **or** 3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

See also Medical Device

DHHS. The Department of Health and Human Services, under the Secretary of Health and Human Services, is responsible for "Improving the health and well-being of America". The National Institutes of Health (NIH), Center for Disease Control (CDC), Health Resources and Services Administration (HRSA) and The Substance Abuse and Mental Health Services Administration (SAMHSA) are examples of DHHS agencies.

Dietary Supplement. Congress defined the term "dietary supplement" in the Dietary Supplement Health and Education Act (DSHEA) of 1994. A dietary supplement is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. They can also be in other forms, such as a bar, but if they are, information on their label must not represent the product as a conventional food or a sole item of a meal or diet. Whatever their form may be, DSHEA places dietary supplements in a special category under the general umbrella of "foods," not drugs, and requires that every supplement be labeled a dietary supplement. If a research study is intended to show a certain health benefit, the supplement may be subject to regulation as a drug in that the study is considered to be designed to make a Drug Claim.

Diminished Autonomous Decision-Making Capacity (DADMC). Refers to a person

with limits in either mental capacity or voluntariness. Mental capacity is the ability to understand and process
information. Voluntariness is the freedom from the control or undue influence of others. A person has

full autonomy when he/she has the capacity to understand and process information, and the freedom to volunteer for research without coercion or undue influence from others.

Subjects with diminished autonomous decision-making capacity who have not been determined to have Impaired Decision-Making Capacity, Incapacitated or Incompetent, are capable of giving informed consent for research.

Directed (For-Cause) Audit/Review. An audit of research and/or investigators initiated at the request of the IRB or Institutional Official to obtain or verify information necessary to ensure compliance with regulations and institutional requirements and to inform decisions about the conduct of human subjects research and/or human subjects protection.

Disapproved. An IRB action taken when the determinations required for approval of research cannot be made, even with substantive clarifications or modifications to the protocol and/or informed consent process/document. *Note: Research cannot be disapproved by expedited review.*

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

Dissent. Behaviors that would indicate an individual does not want to participate (Where seeking assent, dissent behaviors may be interpreted in certain studies as simply moving away, certain facial expressions, head movements, etc.)

Documentation. The act or an instance of furnishing or authenticating with documents. Documentation of informed consent includes use of a written consent form, approved by the IRB and signed and dated by the subject or the subject's legally authorized representative.

Drug. A drug is defined as:

- A substance recognized by an official pharmacopoeia or formulary.
- A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
- A substance (other than food) intended to affect the structure or any function of the body.
- A substance intended for use as a component of a medicine but not a Device or a component, part or accessory of a Device.
- Biological products are included within this definition and are generally covered by the same laws and regulations, but differences exist regarding their manufacturing processes (chemical process versus biological process).

Drug Claim. Is that the product is useful in diagnosing, mitigating, treating or curing a specific disease or class of diseases. Nutrient content claims characterize the level of a nutrient in a food (e.g., "high in fiber"). Health claims describe the role of a food substance in reducing the risk of a disease (e.g., "Adequate folate in healthful diets may reduce a woman's risk of having a child with a brain or spinal cord birth defect. "). If a research study is intended to show a certain health benefit, care should be taken to consider whether the research is intended to claim that a Dietary Supplement is useful in diagnosing, mitigating, treating or curing a specific disease or class of diseases, as these are drug claims, not health claims Dietary supplements that bear such disease claims are subject to regulation as Drug.

The Investigation / Investigational use of approved, marketed Drug products to develop information about the product's safety or efficacy differs from the situation for food products or Nutritional Supplement used in scientific studies to develop information to support a “health claim”. "Investigational use" of an approved drug product suggests the use in the context of a clinical study protocol, see 21 CFR 312.3(b). When the principal intent of the investigational use of a drug or device test article is to develop information

about the product's safety or efficacy, submission of an IND or IDE may be required unless certain criteria are met. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA), the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market as well as reviewing safety information in 75-day premarket notifications for new dietary ingredients, to ensure that such products are reasonably expected to be safe (21 CFR 190.6). As of August 24, 2007, manufacturers of dietary supplements are required to follow current good manufacturing practices (cGMPs) for dietary supplements, known as the Final Rule cGMPS For Dietary Supplements.

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Elements of Informed Consent. No investigator may involve a human being as a subject in research covered by UT Southwestern policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

(a) Basic required elements of informed consent. Except when waiver or alteration is sought and approved by the IRB, in seeking informed consent, the following information

is required to be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

A description of any reasonably foreseeable risks or discomforts to the subject;

(2) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(3) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(4) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(5) For research involving **more than minimal risk**, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(6) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(7) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(b) Additional elements of informed consent.

When appropriate (in part based on risk and complexity of the study), one or more of the following elements of information are required (NOTE: “required by the IRB when appropriate” means that after approval, they are considered part of the list of required elements that must be considered in the discussion of consent form changes that would not constitute a minor change) to be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

Eligibility Criteria. Summary criteria for participant selection. See Inclusion/Exclusion Criteria

Embryo. Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early

pregnancy (i.e., from conception to the eighth week of pregnancy).

Emergency research. Planned research involving human subjects who have a life-threatening medical condition that necessitates urgent intervention (for which available treatments are unproven or unsatisfactory), and who, because of their condition (such as traumatic brain injury) cannot provide informed consent.

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

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

Emergency Use. Emergency Use of an unapproved drug (i.e., Emergency IND or Emergency Protocol) or device (Emergency Use)

When an unapproved drug or device was used to treat a patient emergency situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. The FDA definition of an emergency is similar but slightly different for drugs and devices.

Drug – either Life-threatening or Severely Debilitating

- Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be

immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
- For drugs, FDA authorization must be obtained (either telephone or written submission) **prior to use** of a drug.

Device – either life-threatening or serious disease or condition that needs immediate treatment

- For devices, the FDA must be notified within five days. The FDA recognizes that typically there will not be time to obtain prior IRB approval - must be reported within five (5) working days of initiation of treatment.

Emergency Deviation. Any changes to the IRB-approved investigational plan without prior IRB approval intended to eliminate an apparent immediate hazard to subjects or, for IDE studies, to protect the life or physical well-being of a subject in an emergency.

- Examples include withholding study drug in response to a serious adverse event (actual harm) or to avoid a serious harm (risk of harm).

Emergency deviations may also be Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO), which require prompt reporting to the reviewing IRB (and UTSW HRPP for reliance studies).

Employee. Used as a term within the definition of whether an institution is Engaged In Research Individuals (in combination "Employee or Agent"). An employee is a person who is hired for a wage, salary, fee or payment to perform work for an employer. Employees are individuals performing institutionally designated activities and acting on behalf of the institution or exercising institutional authority or responsibility.

Therefore, the critical issue in determining whether an institution is engaged in research is whether the facts indicate that someone is working on the institution's behalf, on their own behalf, or someone else's behalf, when they are performing the research activities in question. In certain cases, even though the individual may be employed in whole or in part by an institution, where the individual is performing research activities outside the institution, outside their affiliation with the institution in question, there exists the possibility that he/she may not be considered an employee or agent of the institution in question where the research activity is concerned since they are not "performing institutionally designated activities and acting on behalf of the institution or exercising institutional authority or responsibility" in that regard. It is possible for a UT Southwestern employee to conduct research and not be considered an agent of the university if the research is conducted during non-official duty time, is not in connection with her/his UT Southwestern responsibilities, is not being conducted at a UT Southwestern facility and the research is not supported by a direct HHS award to UT Southwestern.

The institution however generally reserves the right to determine for themselves whether their employee (in whole or in part) is "performing institutionally designated activities and acting on behalf of the institution or exercising institutional authority or responsibility" in regard to that research and the IRB will generally consider this in determining whether the institution in question is engaged in research.

Employee of a Covered Entity. A covered entity is responsible for civil monetary penalties resulting from HIPAA violations committed by its agents, including employees, independent contractors, and other members of its workforce, therefore where the word employee is used in research policies where HIPAA may be applied, this definition will include such individuals. Note that although a covered entity will not be responsible for violations committed by its business associates, the covered entity must have complied with the HIPAA business associate contractual provisions and must not have known of the pattern of activity or practice of the business associate that resulted in the violation,

or if aware of such pattern or practice, must have made a good faith effort to take appropriate corrective action.

Engaged In Research – Institutions. In general, an institution is considered engaged in a particular non- exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them;

identifiable private information about the subjects of the research; (3) the informed consent of human subjects for the research; 4) whenever the institution receives a direct HHS award to support such research, even if all of the human subjects activities will be performed by agents or employees of another institution 45 CFR 46.102(d),(f).

Institutions that are engaged in non-exempt human subjects research that is conducted or supported by any HHS agency must be covered by an Office for Human Research Protections-approved Assurance Of Compliance. An institution holding an OHRP-approved Federal wide Assurance is referred to as an Assured Institution.

Federally-supported is defined throughout the FWA and the Terms of Assurance as the U.S. Government providing any funding or other support.

An institution may extend its FWA to cover a collaborating individual investigator from a Non-Assured Institutions under certain conditions using the OHRP sample Individual Investigator Agreement (IIA) or a comparable agreement developed by the institution.

For detailed description of when an institution is engaged in research see the OHRP Website, http://www.hhs.gov/ohrp/policy/index.html#engagement.

Engaged In Research Individuals. HRPP has defined when an individual is engaged in research based on the OHRP policy guidance of when institutions are engaged.

In general, individuals are considered engaged in a non-exempt human research project (and therefore would need IRB approval) when their involvement in the human subjects research includes any of the following activities:

- The individual receives an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e., awardee), even where all activities involving human subjects are carried out by individuals of another institution.
- The individual intervenes (see Intervention) for research purposes with any human subjects of the research by performing Invasive or Noninvasive procedures (e.g., drawing blood; collecting buccal mucosa cells using a cotton swab; administering individual or group psychotherapy; administering Drug or other treatments; surgically implanting medical Device; utilizing physical sensors; and utilizing other measurement procedures).
- Individual intervenes for research purposes with any human subject of the research by manipulating the environment (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; and/or orchestrating environmental events or social interactions).
- The individual interacts (see Interaction) for research purposes with any human subject of the research. (e.g., engaging in protocol-dictated communication or interpersonal contact; asking someone to provide a specimen by voiding or spitting into a specimen container; and conducting research interviews or administering questionnaires).
- The individual obtains the informed consent of human subjects for the research.
- Individual obtains for research purposes, Identifiable private information or identifiable biological specimens from any source for the research. Obtaining includes, but is not limited to: (a) observing and/or recording private behavior; (b) using, studying, or analyzing for research

  purposes, identifiable private information or identifiable specimens provided by another institution, and (3) using, studying, or analyzing for research purposes

identifiable private information or identifiable specimens already in the possession of the investigators. **Private information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the investigator either directly or indirectly through coding systems.

Examples of when individuals are **NOT "Engaged"** in non-exempt human research:

- an appropriately qualified laboratory technician from Clements University Hospital performs routine serum chemistry analyses of blood samples for investigators as part of a commercial service.
- a radiology technician from the Dental School performs bite-wing x-rays and sends the results to investigators as a service.
- an individual who only function is to: (a) inform prospective subjects about the availability of the research; (b) provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document)

Enrolled Subject. See Subject Status: Enrolled

Enrollment. The process of seeking eligible participants and obtaining their consent to participate in the research. Enrollment generally starts with recruitment, leading to screening for eligibility, and consent to enroll in the study. *See* Accrual.

Equitable. Fair or just; used in the context of selection of subjects, to indicate that the benefits and burdens of research are fairly distributed.

Ethical Codes and Statements Of Ethical Principles. There are three major ethical codes that provide general ethical guidelines for the responsible conduct of Research in the United States and which provide the basis for the HHS/**FDA** regulations on the protection of human Research subjects. It should be noted that HHS/**FDA** regulations

are not intended to serve as an ethical code. In fact, 45 CFR 46.103 requires each institution's Assurance of Compliance to include a statement of principles for ethical conduct of research which may be based upon "an appropriate existing code, declaration or statement of ethical principles."

Most institutions use the Belmont Report, Declaration of Helsinki and the Nuremberg Code.

Ex-Officio. Member by virtue of the office held.

Exception. A one-time, intentional action that departs from the IRB approved protocol for a single subject. An exception is identified before it occurs and is under the control of the investigator.

Single subject exceptions may not be initiated without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject.

Examples include (but are not limited to): enrollment of a single subject who does not meet all eligibility criteria for a study, but the investigator and sponsor have agreed this subject should be enrolled.

Exculpatory Language. As it applies to informed consent, any written or verbal communication through which a research participant (or his/her legally authorized representative) is asked to waive or appear to waive any of the participant's legal rights or to release (or appear to release) the investigator, sponsor, or institution or its agents from liability for negligence.

Exempt human subjects research. Research that involves human subjects that is not subject to regulations requiring IRB review and approval. Categories of research activities that may be determined to be exempt from review by the IRB are defined by

federal regulations and UT Southwestern policy. *Note: Investigators performing exempt research must comply with the requirements of the HRPP even when the research is exempt.*

Exempt Review. What Exemption Means: "Exemption" as used in this document means exemption from the requirements set forth in Regulations for the Protection of Human Subjects (45 CFR 46), such as the requirement for a written informed consent document. What Exemption Does Not Mean: "Exemption" does not mean that the research activity is exempt from the law, and it does not mean that the research need not conform to the canons of sound research ethics. In order to qualify for exemption, a research study must fall entirely within one or more of the six categories for exemption and it cannot place subjects at greater than minimal risk. If the research involves prisoners, then it does not qualify for exemption from federal regulations and IRB review.

Existing Data/Specimen. Data/specimen in the records or on the shelf prior to IRB review and was created for a reason other than the proposed research. All data included in the request to analyze existing data must exist at the time the research is proposed.

Expanded Access: The use of an investigational medical product (i.e. one that has not received FDA approval), outside of a clinical trial, for the diagnosis, monitoring, or treatment of a serious disease or condition. It is also known as “compassionate use”.

Expedited Research. Non-exempt human research that is eligible for Expedited Review Of Research.

Expedited Review of Research. Procedure used to review either or both of the following:

- Some or all of the research appearing on HHS list of categories of research, as published in the Federal Register, and found by the reviewer to involve no

more than minimal risk.

- Minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized.

Experienced IRB Member: Member who has served for 1 year as an IRB member, or holds a CIP certification, or has 1 year of work experience within an IRB/HRPP office as a coordinator, analyst or a director. Experienced IRB members may be nominated by the HRPP Director and appointed by the IRB Chairs to serve as an expedited reviewer on behalf of each IRB.

Experimental. Term often used to denote a therapy (Drug, Device, procedure, etc.) that is unproven or scientifically yet to be validated with respect to safety and efficacy. Often used to denote FDA approval has not yet been obtained. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness.

Experimental subject: Involves any activity, for research purposes, where there is an intervention or interaction with a human subject for the primary purpose of obtaining the effect of the intervention of interaction (32 CFR 219.102(f)).

Expiration Date. The date that the IRB's approval of research has lapsed and research can no longer be performed. *Note: An expiration date may not be longer than one year from the date the approval period begins.*

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

Exploitation. When one has unfair advantage over another. Often raised as a concern when paying (offering Inducements to) vulnerable populations (e.g., economically disadvantaged or institutionalized individuals). Paying economically disadvantaged individuals the same amount as would be paid to others who are not disadvantaged may be seen as unduly influential. However, paying these individuals less to reduce Undue Influence may be seen as exploitative.

External. As it relates to adverse events and unanticipated problems, external refers to those events or problems experienced by subjects enrolled by investigator(s) approved by IRBs other than the UT Southwestern IRB, to perform research at their respective

institutions. These reports might be received as part of a multicenter clinical trial, because a local site/institution has obtained UT Southwestern IRB approval, or even if not part of the same trial if the external event involves an FDA-regulated item under investigation at a local site/institution that has obtained UT Southwestern IRB approval.

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Family Member. For purposes of the waiver of informed consent for emergency research, any one of the following legally competent persons: spouse, parent, child (including an adopted child), brother, sister, spouse of a brother or sister, and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

FDA. US Food and Drug Administration, an agency of the Federal government, established by Congress in 1912 and presently part of the Department of Health and Human Services (HHS).

FDA Approved. Approved or cleared by the FDA is a general term in which FDA regulated articles which have been submitted to the FDA have been reviewed and resulted in any of the following:

> Drugs, Biologics: FDA Approved or cleared refers to FDA having issued premarketing approval (PMA)
>
> Devices: FDA Approved or cleared refers to FDA having issued a pre-market approval (PMA); cleared the device for marketing via a Premarket Notification 510(k); considered the device exempt under 510(k) (807.85).

FDA Regulatory Paths To Market Devices: Three regulatory paths to the market for devices are via Premarket Approval (PMA), Premarket Notification (510(k)), and HDE (see a brief description below).

A device with an approved PMA is approved for marketing based on valid scientific evidence and reasonable assurance that the device is safe and effective for its intended use. Once approved, it can be marketed and sold within its approved labeling. There are no restrictions on the price, and it can be used by anyone qualified to use the device.

A 510(k) device is cleared for marketing when the agency finds that it is at least as safe and effective, that is, substantially equivalent, to a legally marketed device that is not required to have a PMA. Using valid scientific evidence, submitters compare their device to one or more similar legally marketed devices, comparing the indications for use and technological characteristics.

A device with an approved HDE is approved for marketing, but the approval is based on evidence of safety and probable benefit. The Act and implementing regulations exempt HUDs from the requirement to establish a reasonable assurance of effectiveness. The HUD is intended for use in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the US per year.

FDA-Regulated Human Research. Human research will be considered FDA-regulated and therefore may be subject to FDA regulations (including but not limited to those) specific to:

1. informed consent
2. IRB review and
3. drugs, biologics or devices as appropriate) when the human research activity is Human Research according to FDA Regulations.

Human research is considered FDA regulated when the activity involves an FDA-regulated test article and the activity involves human participants.

An activity involves an FDA regulated test article when one or more of the following is true:

- The activity involves the use of a Drug, or other than the use of a marketed drug in the course of medical practice; **or**
- The activity involves the use of a Device to evaluate safety or effectiveness of that device; **or**
- Data from the activity will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA-Regulated Product.

An activity involves human participants when one or more of the following is true:

- The test article will be used on one or more humans; **or**
- Data obtained from controls will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA regulated product; **or**
- Data obtained from use of a device on tissue specimens will be submitted to, or held for inspection by, the FDA in support of a marketing or research application for an FDA regulated product.

FDA-Regulated Product. Used in human research involves any product (e.g., food including dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, biological products for human use, medical device for human use or electronic products,) used in or being developed for use in man. The FDA is responsible for determining whether sufficient evidence exists for such products to be claimed as safe and effective. For the purposes of human research, the term is often used to clarify when human research, in addition to being subject to other federal regulations, also falls under the FDA research regulations.

Feasibility Study. "Feasibility studies are pieces of research done before a main study to answer the question 'Can this study be done?' They are used to estimate important parameters that are needed to design the main study". Data collected would not be analyzed or included in publications. Feasibility studies typically do not meet the definition of research involving human subjects and therefore would not require IRB review.

Examples:

1. Going to a potential site to see if the research is possible
2. Checking to see what is the best approach to the research
3. Going through a consent process with friends to see if the information is comprehensible
4. Sending your survey instrument to a few experts in the field for their feedback as to whether or not the questions are appropriate for the topic and/or cohort of the research
5. Feedback from colleagues and peers about research design
6. Student researcher designs questionnaire for their study's target population and asks someone from a different population to test the questionnaire

Federalwide Assurance (FWA). The Federalwide Assurance (FWA) is the only type of new Assurance Of Compliance accepted and approved by OHRP for institutions engaged in non-exempt human subjects

research conducted or supported by HHS (DHHS). Under an FWA, an institution commits to HHS that it will comply with the requirements set forth in 45 CFR part 46, as well as the Terms of Assurance.

Fetus. Unborn child; the product of conception from implantation until delivery.

Final report. A report the principal investigator may elect to submit to the IRB to serve as a final record of any pertinent activity since the last continuing review report and to

record research project completion.

Final Rule CGMP For Dietary Supplements. The U.S. Food and Drug Administration issued the final rule establishing regulations to require current good manufacturing practices (CGMPs) for dietary supplements. The final CGMP is effective August 24, 2007. To limit any disruption for Dietary Supplement produced by small businesses, the rule has a three-year phase-in for small businesses. Companies with more than 500 employees have until June 2008 to comply, companies with less than 500 employees have until June 2009 to comply, and companies with fewer than 20 employees have until June 2010 to comply with the regulations. If a research study is intended to show a certain health benefit the a dietary supplement may be subject to regulation as a Drug in that the study is considered to be designed to make a Drug Claim.

Financial Sponsor. The agency, organization, company, or person that pays for the trial.

Finder's Fee. Compensation of any type (e.g. cash, cash equivalents, office or medical supplies, educational stipends, gift certificates, travel cost in excess of normal reimbursement costs, or anything else of value) to an individual made in exchange for referral or recruitment of a participant to a research study. Such payments, generally, are made to study team members who are in a position to identify potential participants who might qualify for enrollment into a study. The finder's fee is paid to the study team member for each participant they recruit who actually enrolls in the study. It is not permissible to pay or accept "finder's fees" at UT Southwestern. Additionally, it is not permissible for UT Southwestern employees or students to accept personal payments from sponsors or others in exchange for accelerated recruitment or referrals of patients. This does not include compensation for services rendered which include screening and referral activity unrelated to whether the participant ultimately enrolls in or completes the research study.

Finding of noncompliance. An occurrence or determination of noncompliance that

does not require further confirmation or investigation (e.g., failure to respond to the IRB within established deadlines, allegation of noncompliance determined by the IRB to be true).

Food and Drug Administration (FDA). The regulatory authority in the United States that oversees the pharmaceutical and medical device industries. The FDA is responsible for ensuring that the drugs and medical devices marketed in the U.S. are safe and have a greater benefit than risk when used according to manufacturer's directions.

For-Cause Audit/Review. An audit of research and/or investigators initiated at the request of the IRB or Institutional Official to obtain or verify information necessary to ensure compliance with regulations and institutional requirements and to inform decisions about the conduct of human subject research and/or human subject protection.

Foreign adversary. The United States Secretary has determined that the following foreign governments or foreign non-government persons have engaged in a long-term pattern or serious instances of conduct significantly adverse to the national security of the United States or security and safety of United States persons and, therefore, constitute foreign adversaries solely for the purposes of the Executive Order, this rule, and any subsequent rule:

1. The People's Republic of China, including the Hong Kong Special Administrative Region and the Macau Special Administrative Region (China);
2. Republic of Cuba (Cuba);
3. Islamic Republic of Iran (Iran);
4. Democratic People's Republic of Korea (North Korea);
5. Russian Federation (Russia); and
6. Venezuelan politician Nicolás Maduro (Maduro Regime).

Full board review. Studies reviewed by the full, convened IRB committee with a recorded vote and corresponding minutes to document the discussion. Review of proposed research at a convened meeting at which a majority of the membership of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.

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Generalizable Knowledge. Knowledge that is universally or widely applicable.

Genetic Information Nondiscrimiation Act (GINA). Created in 2008, this act prohibits discrimination in health insurance and employment through the use of genetic information.

Genomic sequencer. Any device/platform used for genome sequencing or research. Texas House Bill 130 § 174.002

Genomic sequencing. Determines identity/order of nucleotide bases. Texas House Bill 130 § 174.002

Good Clinical Practice (GCP). A standard established by the International Conference on Harmonisation for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. *Note: In the United States, FDA has adopted GCP as guidance.*

Guardian. An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. [21 CFR §50.3(s)]

A guardian also means an individual who is authorized to consent on behalf of a child to participate in research. [21 CFR§50.3(s)]

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. [45 CFR §46.402(e)

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Halt. (to research) is a cessation of some or all research activities voluntarily initiated by the Principal Investigator or sponsor (for example temporarily stopping enrollment or other research procedures, placing the study “on hold”). This does not constitute IRB Suspension Of Research or Termination.

Handicapped. Handicapped person means any person who has a **Physical Or Mental Impairment** that substantially limits one or more **major life activities**, has a record of such an impairment, or is regarded as having such an impairment by criteria (for evaluating the subject during the screening process or scheduled evaluations during a research study) established in the research protocol that represent a

need for additional safeguards for vulnerable populations described by the PI in the research protocol or as determined by the IRB (possibly including Diminished Autonomous Decision-Making Capacity (DADMC) if the physical or mental impairment leads to a decreased capacity to make their wishes known).

As used in this research definition of handicapped, the phrase:

1. **Physical or mental impairment** includes as described below impairment that represent a need for additional safeguards for vulnerable populations described by the PI in the research protocol or as determined by the IRB (possibly including Diminished Autonomous Decision-Making Capacity if the physical or mental impairment leads to a decreased capacity to make their wishes known)-

    - Any physiological disorder or condition, cosmetic disfigurement, or anatomical loss affecting one or more of the following body systems: Neurological; musculoskeletal; special sense organs; respiratory, including speech organs; cardiovascular; reproductive; digestive; genitourinary; hemic and lymphatic; skin; and endocrine; that represent a need for additional safeguards for vulnerable populations
    - Any mental or psychological disorder, such as mental retardation, organic brain syndrome, emotional or mental illness, and specific learning disabilities. The term "physical or mental impairment" includes, but is not limited to, such diseases and conditions as orthopedic, visual, speech, and hearing impairments, cerebral palsy, epilepsy, muscular dystrophy, multiple sclerosis, cancer, heart disease, diabetes, mental retardation, emotional illness, and drug addiction and alcoholism that represent a need for additional safeguards for vulnerable

2. **Major Life Activities** includes functions such as caring for one's self, performing manual tasks, walking, seeing, hearing, speaking, breathing, learning, and working.

Health Information. Any information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual. This constitutes a larger set of information which may be broken down into that health information which is not identifiable and that which is Identifiable Health Information. See Individually Identifiable Health Information.

Health Insurance Portability and Accountability Act of 1996 (HIPAA). The HIPAA Privacy Rule regulates the use and disclosure of Protected Health Information (PHI) held by "covered entities" (generally, employer sponsored health plans, health insurers, and medical service providers that engage in certain transactions). By regulation, the DHHS extended the HIPAA privacy rule to independent contractors of covered entities who fit within the definition of "business associates". PHI is any information held by a covered entity which concerns health status, provision of health care, or payment for health care that can be linked to an individual. This is interpreted rather broadly and includes any part of an individual's medical record or payment history. They also must disclose PHI when required to do so by law, such as reporting suspected child abuse to state child welfare agencies.

Health Surveillance. Is an ongoing part of the medical care and public health care functions closely integrated with timely dissemination of these data to those responsible for preventing and controlling disease or injury (may include emergent or urgently identified or suspected imminent health threats to the population to document the existence and magnitude). Generally, not considered a research activity.

HHS (DHHS). Health and Human Services (HHS) or The Department of Health and Human Services, under the Secretary of Health and Human Services, is responsible for "Improving the health and well-being of America". The National Institutes of Health (NIH), Center for Disease Control (CDC), Health Resources and Services Administration (HRSA) and The Substance Abuse and Mental Health Services Administration (SAMHSA) are examples of DHHS agencies.

Health Insurance Portability and Accountability Act (HIPAA). Passed by congress in 1996, this establishes the United States' standards for the protection of health information and makes it easier for people to keep health insurance, protect the confidentiality and security of healthcare infomraiton, and help the healthcare industry control administrative costs.

HIPAA authorization. A customized document or form that gives permission to use specified protected health information (PHI) for a specific purpose, or to disclose PHI to a third party specified by the investigator other than for treatment, payment or health care operations.

HRPP Policies and Procedures. Policies and procedures of the Office of Human Research Protection Program and IRBs that apply to the conduct, review, and oversight of human subjects research and describe the roles and responsibilities of those involved in these activities.

HUD Clinical Investigation. Once a HDE is granted, and if a clinical investigator or the HDE holder wants to conduct a clinical investigation (i.e., research study) using the HUD.

An HDE holder may collect safety and effectiveness data for the HDE-approved indication(s) without an IDE. While this is a clinical investigation, FDA considers the study exempt from the requirement of 21 CFR Part 812 as long as the HUD is being studied in accordance with the approved indication(s) described in labeling, because the HUD as such is legally marketed and can be lawfully shipped without an IDE. See 21 CFR 812.1. IRB approval (21 CFR Part 56) and informed consent (21 CFR Part 50) are still required for these studies, however, because they are FDA-regulated clinical investigations

Human Subject. *Pre-2018 Common Rule Definition:* "An individual who is or becomes a participant in Research, either as a recipient of the Test Article or as a control. A subject may be either a healthy individual or a patient." (21 CFR 56.102(e)) For research involving a Medical Device, a human subject means "A human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease." (21 CFR 812.3(p))

2018 Common Rule Definition: A living individual about whom an investigator (whether professional or student) is conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Human Subject Research. Research involving Human Subject.

Humanitarian Use Device Exemption (HDE). Is an application to the FDA that is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of sections 514 and 515 of the Food, Drug, and Cosmetic Act (the Act). FDA approval of an HDE authorizes an applicant to market a Humanitarian Use Device Humanitarian Use Device (HUD), subject to certain profit and use restrictions set forth in section 520(m) of the Act (i.e., HUDs cannot be sold for profit except in narrow circumstances and they can only be used in a facility after an IRB has approved their use in that facility, except in certain emergencies). An HDE approval is based on safety and probable benefit. HDEs are exempt from the requirement to provide a reasonable assurance of effectiveness as required in Investigational Device Exemption (IDE) applications. The person who obtains the Humanitarian Device Exemption (HDE) from FDA is the HDE holder.

The FDA will consider an HDE application for any of the following:

- no comparable device is available to treat or diagnose the disease or condition; or
- a comparable device is available under another approved HDE application; or
- a comparable device is being studied under an approved Investigational Device Exemption (IDE) (21 CFR 814.104(b)(2)).

If a comparable device with the same indications for use is marketed through either the premarket approval (PMA) process or the premarket notification (510(k)) process, a new HDE for a HUD device cannot be granted by the FDA.

Humanitarian Use Device (HUD). A device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect (or are manifested in) fewer than 4000 individuals in the US per year.

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Identifiable. Identifies the individual; or with respect to which there is a reasonable basis to believe the information can be used to identify the individual. Not all identifiable information is necessarily Identifiable Health Information. Individually Identifiable Health Information. This would only be the case if it was actually associated with Health Information.

Identifiable Data/specimens are generally identifiable health information and are either:

Coded samples – sometimes termed “linked” or “identifiable”, are those from identified materials with a code rather than a name or any other personal identifier such as a patient number, where the source retains information linking the code to particular human materials or where the extent of the clinical or demographic information provided with the sample is sufficient that the investigator, the repository, or a third party could link the biological information derived from the Research with material from a particular person or a very small group of identifiable persons. If the key is destroyed or not accessible by the investigator or repository, then it is possible that these samples would then be considered de-identified coded samples but they would be identifiable health information until this occurred.

or

Identified samples - are those samples supplied from identified materials with a personal identifier sufficient to allow the biological information derived from the research to be linked directly, with the particular person from whom the material was obtained.

Identifiable Biospecimen. *2018 Common Rule Definition:* A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Identifiable Private Information. *2018 Common Rule Definition:* Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

Identified Prospective Subject. *See* Subject Status.

Immediately Life-Threatening Disease. Means a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

Impaired consent capacity. A person lacking the ability based on reasonable medical judgment to understand and appreciate the nature and consequences of a treatment decision, including the significant benefits and harms of and reasonable alternatives to any proposed treatment decisions. Also see Incapacitated. Subjects who have impaired decision-making capacity are not capable of giving informed consent for research but may be capable of providing assent.

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.

In Vitro. Literally, “in glass” or “test tube” – used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from *in vivo*.

In Vivo. In the living body; processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory.

Incapacitated. A person lacking the ability based on reasonable medical judgment to understand and appreciate the nature and consequences of a treatment decision, including the significant benefits and harms of and reasonable alternatives to any proposed treatment decisions. Also see Impaired Decision-

Making Capacity. Subjects who are incapacitated are not capable of giving informed consent for research but may be capable of providing assent.

Incidents, Experiences OR Outcomes. Are general sources of information that may indicate an **actual harm** has occurred or that there is an **increased risk of harm**.

Information of **actual harm** can be:

- an Adverse Event (encompassing both physical and psychological harms); or
- a problem or event not considered an adverse event** (encompassing social or economic harms) Information indicating an **increased risk of harm** is:
- a problem or event not considered an adverse event** that place subjects or others at increased Risk of harm than was previously known or recognized, but no harm occurred.

[** referred to as "*non-AE incidents, experiences or outcomes*"]

Inclusion/Exclusion Criteria. The medical or other standards determining whether a person may or may not be allowed to enter a research study. 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.

Incompetent. Referring to a person who is not able to manage his/her affairs due to mental deficiency (low IQ, deterioration, illness or psychosis) or sometimes physical disability and who has been appointed a guardian or conservator by a legal determination.

Persons determined to be legally incompetent are unable to provide Informed Consent or Legally Effective Informed Consent. They may be able to provide assent.

[Incompetent is legal term removed from Texas Probate Code in 1993 but still used in various federal regulations (e.g., 38 CFR concerning guardian). Texas state law now uses the term "Incapacitated."]

Individual Investigator Agreement (IIA). An agreement between an Assured Institution and a Collaborating_Individual_Investigator or Collaborating Institutional Investigator that permits the assured institution to extend its Federalwide Assurance to cover the investigator.

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

Individually Identifiable Private Information. Private Information or Specimens are individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Private information or specimens are not individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. For example, if the following conditions are both met:

1. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
2. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:

    - the key to decipher the code is destroyed before the research begins;
    - the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
    - there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
    - there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

Inducements. Are offers that get people to do things they may not otherwise do. Inducements or incentives, rewards or payments may be acceptable depending on the

population, level and type but they may also be considered Undue Influence if the reward/payment is so large as to persuade the person to take undue risks or volunteer against their better judgment. Another concern about undue influence (unacceptable inducements) is they can result in a subject lying or concealing information that may otherwise exclude them from the research. As a result, if the study involves no risk or minimal risk, the concern over undue influence is reduced. The IRB should consider ways to reduce the influence of payments or rewards that undermine a person's capacity to exercise free choice and could invalidate consent. The IRB should balance the need to reduce undue influence with the need to avoid Exploitation of populations.

Or, Potential For Undue Influence.

Informed Consent. A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in Research or to undergo a diagnostic therapeutic or preventive procedure. For the purposes of contrast, "Consent," is voluntary agreement without mention of whether full knowledge was imparted or understanding took place and "Legally Effective Informed Consent" is obtained when a subject or a subject's legally authorized representative as outlined in 45 CFR 46 (Common Rule) agrees to participate. Informed Consent (often used as a variation of "consent" or "legally effective informed consent") is obtained only after the prospective subject is provided sufficient opportunity to consider whether or not to participate. Neither, informed consent nor legally effective informed consent can be obtained from a subject with Diminished Autonomous

Decision-Making Capacity (DADMC) for research purposes (Surrogate Consent or Legally Authorized Representative (LAR) is obtained in such a case).

Initial Review Of Research. The review of new, not previously approved research including new studies tabled/deferred at previous meetings.

Innovative Therapy. Innovative therapy represents a deviation from standard medical practice. Physicians are free to innovate if the innovative procedure is applied solely to enhance the well- being of their patient. However, when innovative therapy differs significantly from routine practice it should be viewed and treated as experimental, with appropriate safeguards in place to protect the rights and welfare of the patients (subjects) (e.g., RSRB review, informed consent, etc.). In order to validate innovative therapy, the innovative procedure should be subjected early on to an evaluation via a formal Research protocol.

Institution. Any public or private entity or agency (including federal, state or other agencies).

Institutional official. The institutional official (IO) who is the signatory on the federalwide assurance (FWA) filed with OHRP to ensure compliance with regulations governing protection of human subjects. OHRP requires the institutional official to be a high-level official who has the authority to represent the institution named in the FWA.

Institutional Review Board (IRB). The institutional review board is a federally mandated, institution- designated regulatory body empowered to oversee Human Subject Research.

- Internal IRB – for UT Southwestern, the UT Southwestern IRB's
- External IRB – for UT Southwestern, any IRB managed by another organization

Institutionalized. Confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (e.g., a psychiatric hospital, home or school for the retarded).

Also see, Mentally Disabled.

Interaction. Communication or interpersonal contact between an investigator and participant.

Internal Event. As it relates to adverse events and unanticipated problems internal refers to those events or problems experienced by subjects enrolled by the investigator(s) approved by the UT Southwestern IRB to perform research at their respective institutions.

Also, Adverse Event *or* UPIRSOs.

Intervention. *Pre-2018 Common Rule Definition:* Includes both physical procedures by which data are gathered (for example, venipuncture) and manipulation of the subject or the subject's environment that are performed for research purposes.

2018 Common Rule Definition: Both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interventional Study. A clinical study in which participants **are assigned to receive** one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol.
Participants may receive diagnostic, therapeutic, or other types of interventions.

Also see, Clinical Trial.

Interventional Study Phase (s). The phase of investigation including:

> **Phase 0**: exploratory trials, involving very limited human exposure, with no therapeutic or diagnostic intent (e.g., screening studies, microdose studies). See FDA guidance on exploratory IND studies for more information.

Phase 1: includes initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients

Phase 1/Phase 2: for trials that are a combination of phases 1 and 2

Phase 2: includes controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks

Phase 2/Phase 3: for trials that are a combination of phases 2 and 3

Phase 3: includes expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling

Phase 4: studies of FDA-approved drugs to delineate additional information including the drug's risks, benefits, and optimal use

Interventional Study Purpose. The reason for the protocol.

- **Treatment**: protocol designed to evaluate one or more interventions for treating a disease, syndrome or condition
- **Prevention**: protocol designed to assess one or more interventions aimed at preventing the development of a specific disease or health condition
- **Diagnostic**: protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition

- **Supportive Care**: protocol designed to evaluate one or more interventions where the primary intent is to maximize comfort, minimize side effects or mitigate against a decline in the subject's health or function. In general, supportive care interventions are not intended to cure a disease.
- **Screening**: protocol designed to assess or examine methods of identifying a condition (or risk factors for a condition) in people who are not yet known to have the condition (or risk factor).
- **Health Services Research**: protocol designed to evaluate the delivery, processes, management, organization or financing of health care.
- **Basic Science**: protocol designed to examine the basic mechanism of action (e.g., physiology, biomechanics) of an intervention.

Invasive. Invasive is considered to be entering the body via puncture or incision or requiring numbing or sedative medication for insertion into the body.

Note: Noninvasive does not always constitute minimal risk.

Examples of invasive procedures are those that: 1) penetrate or pierce the skin (except for simple venipuncture) 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.

Clarification: For procedures already being performed for standard care purposes: It is possible to consider a procedure to be noninvasive if performed in addition to the usual activities performed during a standard care invasive procedure so long as the additional activity does not require further puncture or incision or require additional numbing or sedative medication for further insertion into the body. This does not mean

the procedure qualifies as minimal risk simply by meeting the definition of noninvasive as extending the standard care procedure time or investigational nature of a device used in that activity might add risk to the standard procedure. Risk determination is a separate criterion for the purposes of Expedited Review for example or for the purposes of determining whether a Diagnostic device is exempt from submission to the FDA for an IDE.

Investigation / Investigational. Investigation is a term used by the FDA concerning activities subject to FDA regulations and means a 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 FFD&C Act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit) or Research involving one or more subjects to determine the safety or effectiveness of a drug, biologic or device. The terms research, clinical research, clinical study, study, and Clinical Investigation are deemed to be synonymous for purposes of the FDA.

Investigational agent. A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or

assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication or products used to gain further information about an approved use.

Investigational Device. Includes unapproved devices and some approved devices:

A Device not yet approved for marketing by the FDA when used in research, see Clinical

Investigation, involving one or more subjects to determine the safety or effectiveness of a device is an investigational device.

Also, any medical device, including **approved devices** or transitional devices (devices previously approved as a drug (before 1976)), **are** Investigation / Investigational **devices if they are the object of a** Clinical Investigation (abridged: research involving one or more subjects to determine the safety or effectiveness of a device). They may then be considered exempt from certain FDA regulations (e.g. 21 CFR 812) in certain circumstances but they remain investigational devices if they are the object of the study and the study in most cases remains subject to other FDA regulations (e.g., 21 CFR 50 and 56).

Investigational Device Exemption (IDE). An IDE is like an IND for a new drug. It allows an unapproved medical Device to be shipped for use for Investigation / Investigational purposes. It is also required when an FDA approved or FDA cleared device is used in a Clinical Investigation for the purposes of testing safety or effectiveness (unless exempt from prior submission for the IDE or where abbreviated requirements may be allowed) where the intent is for the data to be included in a submission to the FDA or may later be held for inspection by the FDA. FDA has 30 days to review the IDE request and notify the sponsor if approval is withheld. The requirements for an IDE are similar to an IND and are designed to ensure that the sponsor conducts adequate preclinical testing, selects appropriate subjects for clinical Research, obtains IRB approval, obtains adequate informed consent, uses qualified investigators, monitors the investigation, and collects data promptly. In deciding whether to approve an IDE, the FDA focuses on how the investigation will be conducted rather than on a precise risk-benefit analysis. The IDE regulation is 21 CFR 812 (45 Fed Reg 3751, January 19, 1980).

Under abbreviated requirements when medical Device are classified as non-significant risk (NSR) by the sponsor and the IRB agrees, the investigation may begin without prior submission of an IDE. Under the abbreviated IDE requirements, the device is considered

to have an approved IDE issued by the IRB. If, however, the IRB determines the Device to be a significant risk (SR) device, an IDE must be submitted and approved before the study can be initiated. In this circumstance, it does not matter if the sponsor has classified the device as NSR.

Investigational Drug. Includes those substances in any of the clinical stages of evaluation which have not been released by the FDA for general use or cleared for sale in interstate commerce. An investigational drug may also be defined by one of the following:

1. A drug in any of the clinical stages of evaluation (Phase I, II, III) which has not been released by the FDA for general use or cleared for sale in interstate commerce.
2. Any commercially available drug proposed for a new use.
3. A new dosage form or method of administration.
4. A commercially available drug which contains a new component such as an excipient, coating or menstruum.
5. A new combination of two or more commercially available drugs.
6. A combination of commercially available drugs in new proportions.

Investigational New Drug - Exemption (IND). An IND (Form FDA 1571) is an application filed (usually by the sponsor) with the FDA that includes a detailed description of the planned investigation including Phase I, II and III studies. The application must also contain names and addresses of the investigators and identification of the IRB responsible for initial and continuing review and approval of the proposed study. The FDA has 30 days to review the IND and notify the sponsor if approval is withheld. The applicable FDA regulation for INDs is 21 CFR 312.1. Each investigator who will participate in the study must provide the sponsor with a completed Statement of Investigator (Form FDA 1572) as required by 21 CFR 312.53(c).
This form addresses investigator training and experience as well as investigator commitments.

Investigational New Drug Application. Once the clinical evaluation of a drug is completed, an NDA must be submitted to FDA to obtain approval to market the drug. The NDA regulations are 21 CFR 314. In an NDA review there is a much closer scrutiny of the data by FDA to ensure safety and efficacy. In contrast, the IND review requires only enough evidence of effectiveness to justify a clinical trial.

Investigator. A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator. (*Definition from: International Conference on Harmonization Good Clinical Practice*)

Investigator's Brochure (IB). A compilation of the clinical and nonclinical data on the investigational products that is relevant to the study of the investigational product or products in human subjects.

Investigator-Initiated INDs/IDE's. See Sponsor-Investigator.

IRB Authorization Agreement (IAA). An agreement between two institutions where one institution agrees to rely on the IRB from the other institution for the review and continuing oversight of its human research. The agreement can cover all human research conducted by the institution, all human research conducted under the institution's Federalwide Assurance (FWA), a subset of research studies, or a single study. A copy of the IAA is filed with Office of Human Research Protections (OHRP) for Assured Institution.

IRB of Record. Denotes the IRB responsible for approval of a specific research study at a given institution. An institution may rely on any number of IRBs within or outside the institution. If an institution relies on an external IRB, an IRB Authorization Agreement must be in effect.

IRB Project Type. Given the various regulatory responsibilities, there are different types of projects that require IRB approval (not just research) including:

Human Subjects Research – research involving living individuals whenever the investigator obtains private identifiable private information or interacts/intervenes for research purposes. (IRB approval required)

Human Subjects Data or Specimen **Repository** – a special category of human subjects research where data and/or specimens are stored in a bank or repository for use in future research studies. (IRB approval required)

Non-Regulated Research determination – activities that do not meet the regulatory definition of research and do not require IRB approval. Examples include quality improvement, health surveillance, and program evaluation. This application should be submitted if you would like an official determination letter from the IRB Office.

Research Not Involving Humans – research that does not involve "human subjects" as defined by the IRB regulations and does not require IRB approval. Examples include research using leftover, de-identified specimens, cell lines and de-identified materials from a repository. This application should be submitted if you would like an official determination letter from the IRB Office.

Exempt Determination – certain minimal risk human subject research is exempt from the IRB regulations. Examples include retrospective chart review if not recording identifying information, survey of adults, and research comparing educational methods. This application should be submitted if you would like an official determination from the IRB Office.

Treatment Use of a **Humanitarian Device** – humanitarian devices receive a specific FDA approval (HDE) for treating rare conditions. Although not considered research, the FDA requires IRB approval prior to non-emergency use. (IRB

approval required)

Expanded Access to Investigational Drugs or Devices for Treatment – refers to use of an investigational drug or device when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition. The distinction between expanded access and the use of an investigational drug (or device) in the usual studies covered under an IND (IDE) is that expanded access uses are not primarily intended to obtain information about the safety or effectiveness of a test article. Although not considered research, the FDA requires IRB approval prior to non- emergency use. (IRB approval required).

Emergency Use of an unapproved drug (Emergency IND or Emergency Protocol) or device (Emergency Use)

- This application should be submitted to notify the IRB that an unapproved drug or device was used to treat a patient emergency situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval. The FDA definition of an emergency is similar but slightly different for drugs and devices.
- Drug – either life threatening or severely debilitating
    - Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with

      potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life- threatening or to immediately result in death. Rather, the subjects must be in a life- threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
- For drugs, FDA authorization must be obtained (either telephone or written submission) **prior to use** of a drug.

- Device – either life-threatening or serious disease or condition that needs immediate treatment
  - For devices, the FDA must be notified within five days. The FDA recognizes that typically there will not be time to obtain prior IRB approval - must be reported within five (5) working days of initiation of treatment.

J

K

Key Personnel. Term used in federal grant applications to indicate individuals subject to additional conflict of interest rules and reporting. In general, key personnel include any individual responsible for the design, conduct, and reporting of research for a given study. Key personnel may or may not include the following: study staff, investigators, individuals engaged in human research and individuals not engaged in human research.

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Legally Authorized Representative (LAR). A person authorized either by statute or by court appointment to make health care decisions on behalf of another person who is Incapacitated, Incompetent, or has Impaired Decision-Making Capacity. It is not always

required that Informed Consent to participate in research be given by the legally authorized representative if another form of Surrogate Consent is available such as family member consent depending on applicable state law and institutional policy. Consent by a legally authorized representative should involve all the same considerations that informed consent from a competent subject involves.

See 3.2 INFORMED CONSENT BY SURROGATE for specific information on who may serve as a legally
authorized representative or surrogate.

Legally Effective Informed Consent. Is consent of a subject, or if the subject is incapacitated, incompetent, or has impaired decision-making capacity, then the consent of the subject's Legally Authorized Representative (LAR) or surrogate as outlined in 45 CFR 46 (Common Rule). "Consent" is often used as a short version of "Informed Consent" or "Legally Effective Informed Consent". It is not always required that Informed Consent to participate in research be given by the legally authorized representative if another form of Surrogate Consent is available such as family member consent depending on applicable state law, institutional policy and the determination of the IRB. Someone who is Incapacitated, Incompetent, or has Impaired Decision-Making Capacity cannot give legally effective informed consent for research purposes (a Surrogate Consent or Legally Authorized Representative (LAR) is obtained in such a case).

Life-threatening. Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the recipients must be in a life- threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Limited Data Set. Health information that excludes certain direct identifiers, but may

include city, state, and ZIP code; elements of date; and other numbers, characteristics, or codes that cannot be used to identify an individual or the individual's relatives, employers, or household members. *Note: Limited data sets may be used or disclosed for purposes of research with a data use agreement as described by the HIPAA Privacy Rule at 45 CFR Part 164.*

Longitudinal Study. A longitudinal study is an observational research method in which data is gathered for the same subjects repeatedly over a period of time. Longitudinal research projects can extend over years or even decades. In a longitudinal cohort study, the same individuals are observed over the study period

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M

Major Change Or Modification. (to previously approved research)

Any change that does not meet the definition of a minor change or modification to previously approved research, and/or

A modification which in the judgment of the reviewer fundamentally alters the judgments relied upon to make determinations on any of the criteria for IRB approval under 45CFR 46.111 and/or involves modifications which would not be eligible for expedited review (considering risk and expedited review categories 1-9)

Major, Non-Emergency Deviations. See Noncompliance

Material transfer agreement (MTA). A contract that governs the transfer of tangible research materials between two organizations when the recipient intends to use the materials for his or her own research purposes.

Mature Minor. Someone who has not reached adulthood (as defined by state law), but who may be treated as an adult for certain purposes (e.g., consenting to certain types of medical care).

Medical Definition of Quality Assurance. a program for the systematic monitoring and evaluation of the various aspects of a project, service, or facility to ensure that standards of quality are being met.

Medical Device. The Food and Drug Administration (FDA) defines a medical Device as:

An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals.
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

Under FDA regulations governing investigational devices, a clinical investigation may involve human subjects even when the investigational device is used only on unidentified human tissue, blood, or other specimens. For device investigations, a human subject is defined as a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used, or as a control. Consequently, FDA-regulated device studies using identifiable, coded, or

deidentified human specimens may constitute clinical investigations involving human subjects and may require IRB review, even when the research would not be considered human subjects research under the Common Rule.

Before 1976, medical devices could be marketed without review by the FDA. However, in 1976 the medical device amendments of 1976 to the Federal Food, Drug and Cosmetic Act were passes in order to ensure that new devices were safe and effective before they were marketed. The FDA regulations which govern medical devices are 21 CFR 812, 814, 860, 861.

Mental Capacity. *See* Capacity.

Mentally Disabled. Having either a psychiatric disorder (e.g., psychosis, neurosis, personality, or behavior disorder), a developmental disorder (e.g., mental retardation), or a neurological disorder that affects cognitive or emotional functions to the extent that it results in a Diminished Autonomous Decision-Making Capacity (DADMC). Neither, informed consent nor legally effective informed consent can be obtained from a subject with Diminished Autonomous Decision-Making Capacity (DADMC) for research purposes (Surrogate Consent or Legally Authorized Representative (LAR) is obtained in such a case).

See Cognitively Impaired, Diminished Autonomous Decision-Making Capacity (DADMC), Handicapped.

Minimal Risk. "The probability and magnitude of harm or discomfort anticipated in the Research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." For VA studies the determination includes tangible or intangible risk.

Examples of research activities that may well be determined by the Board to involve no more than minimal risk include collection of blood samples from healthy, non-pregnant adults by venipuncture in amounts not exceeding 450 ml in an eight-week period and no more often than two times per week; electrocardiography; electroencephalography; and moderate exercise by healthy subjects. (Examples are not automatically deemed to be of minimal risk simply because they are included on this list).

While the harms and discomforts ordinarily encountered differ widely among individuals and individual populations, an ethically meaningful notion of "harms and discomforts ordinarily encountered" should reflect "background risks" that are familiar and part of the routine experience of life for "the average person" in the "general population." It should not be based on those ordinarily encountered in the daily lives of the proposed subjects of the research or any specific population. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain.)

Minimizing Risk. Federal regulations describe minimizing risks to subjects (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes. Therefore, using the least number of procedures possible to answer the research question is a method of minimizing risk when additional procedures are required. Addressing whether you have minimized risk requires addressing all three aspects of this definition.

Minor. A person who has not attained the legal age of majority under the applicable law of the jurisdiction in which the Research will be conducted (18 years in the state of

Texas), and therefore as a general rule cannot consent to treatment or procedures involved in research. For the purposes of research performed under DHHS regulations Viable Neonates are considered children, whereas neonates of uncertain viability and Nonviable Neonates require additional protections under section B of 45 CFR 46. See 3.2 INFORMED CONSENT BY SURROGATE for specific information on minors and if/when they can give consent to participate in research.

Minor Change or Modification. (to previously approved research)

A modification which in the judgment of the reviewer does not fundamentally alter the judgments relied upon to make determinations on any of the criteria for IRB approval under 45CFR 46.111 does
not adversely impact the overall risk-benefit relationship for the subjects of the research (based on new or modified risk information).

For studies originally approved by expedited review, a minor change is a modification that does not change the study's eligibility for expedited review (considering risk and expedited review categories 1-9).

Minor or Administrative Deviations. See Deviation

Modifications (Changes) Required. An IRB action that specifies conditions under which research can be approved, pending the following: confirmation of specific understandings by the IRB about how the research will be conducted, submission of additional documentation, precise language changes to the

protocol and/or informed consent document(s), and/or substantive changes to documents with specific parameters the changes must satisfy. *Note: Verification that the investigator's response(s) satisfies the conditions for approval set by the IRB may be performed by the IRB Chair and/or other designated individual(s). Also: contingent approval, approval with conditions.*

Modification of Research. *See* Modifications

Multi-Site Research. Research conducted at more than one location and under the jurisdiction of only one IRB.

Multicenter Research. Research conducted at more than one location and under the jurisdiction of more than one IRB.

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N

National Commission. In July 1974, in response to widespread publicity concerning unethical human experimentation in the U.S. (e.g., Tuskegee Syphilis Study, Jewish Chronic Diseases Hospital Study, Willowbrook Study, San Antonio Contraceptive Study), Congress passed the National **Research** Act (Public Law 93-348), which established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral **Research**. The charge of the Commission was to conduct a comprehensive investigation and study to identify the basic ethical principles which should underlie the conduct of biomedical and behavioral Research involving human subjects. Although both **FDA** and HHS had regulations for the protection of human subjects, they were obviously inadequate in light of the many human subject abuses that occurred in medical and

behavioral research conducted in the U.S.

From 1975 through 1978 the Commission published eight reports on various aspects of research involving human beings. These reports formed the basis for the development of the 1981 DHHS and **FDA** regulations. Undoubtedly, the most ethically fundamental report produced by the Commission was the Belmont Report. The other reports produced by the National Commission are: **Research** on the Fetus (1975), **Research** Involving Prisoners (1976), **Research** Involving Children (1977), **Research** Involving Those Institutionalized as Mentally Infirm (1978), Institutional Review Boards (1978), Ethical Guidelines for the Delivery of Health Services by DHEW (1978). The National Commission disbanded in 1978.

National Institute of Health (NIH): A part of the United States Department of Health and Human Services, the NIH is the largest biomedical research agency in the world, comprised of 21 Institutes established between 1937 and 2000.

Neonates. Neonates are newborns who are 28 days old or younger. For the purposes of DHHS regulations viable neonates are considered children and only require the protections under sections A and D of 45 CFR 46 whereas neonates of uncertain viability and nonviable neonates require additional protections under section B of 45 CFR 46.

No-Treatment Control. Placebo Control, No-Treatment Control (suitable where objective measurements are felt to make blinding unnecessary), and dose-comparison control studies are all study designs in which a difference is intended to be shown between the test article and some control. The alternative study design generally proposed to these kinds of studies is an active-treatment concurrent control in which a finding of no difference between the test article and the recognized effective agent (active- control) would be considered evidence of effectiveness of the new agent. There are circumstances in which this is a fully valid design.

Non-Assured Institutions. An institution that does not hold an OHRP-approved Federalwide Assurance is referred to as a non-assured institution. UTSW researchers who conducted Cooperative Research with investigators from non-assured institutions provide additional information to define the responsibilities of each institution. In some cases, an investigator from a non-assured institution may request the UTSW extend its FWA to cover his/her research activities by signing an Individual Investigator Agreement (IIA).

Noncompliance. Any failure to follow:

- Applicable federal regulations, state and local laws, or institutional policies governing human subjects protections, or
- The requirements or determinations of the IRB, including the requirements of the approved investigational plan (e.g., protocol, Smartform, ICD).

Noncompliance can result from performing an act that violates these requirements or failing to act when required.

Non-Scientist. An individual appointed to the IRB who (due to training, background, and/or occupation) is inclined to view research activities from the standpoint of someone outside the scientific or scholarly discipline of the IRB on which he/she serves.

Non-Significant Risk (NSR) Device. Used to define the risk classification of specific devices that do not present a potential for serious risk to the health, safety, or welfare of a subject. Non-Significant risk devices do not include implants, devices that support or sustain human life, or devices that are substantially important in diagnosing, curing, mitigating, or treating disease, or in preventing impairment to human health.

Non-Therapeutic Research. Research that has no likelihood of 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.

Nonviable Neonate. The inability of a baby, in the first 28 days of live birth, to survive outside the womb. In research federal regulations require, after delivery, there must be a determination as to whether the neonate is viable (viable means being able to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. Additionally, there are limitations on determining viability of neonates - individuals engaged in the research may not have any part in determining the viability of a neonate being considered for inclusion in a study. In addition, after delivery, nonviable neonate may not be involved in research unless there is scientific justification for their inclusion, legally effective informed consent of both parents, (exceptions apply, see Research

Involving Pregnant Women, Human Fetuses And/or Neonates) and all of the following additional conditions are met:

(1) Vital functions of the neonate will not be artificially maintained;

(2) The research will not terminate the heartbeat or respiration of the neonate;

(3) There will be no added risk to the neonate resulting from the research;

(4) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) The legally effective informed consent of both parents of the neonate is obtained (waiver or alteration of consent is not allowed). However, there are some exceptions.

Notification. Process of notifying research subjects of changes in the research by letter or phone.

Nuclear Regulatory Commission. The independent government agency established by the Energy Reorganization Act of 1974 to regulate civilian use of nuclear materials.

Nuremberg Code. An international ethical code published in 1947 which established standards for the conduct of Research involving human beings. It arose out of the Nuremberg War Crimes Trial, where 23 Nazis were charged with crimes against humanity that involved murderous pseudomedical experimentation. Twenty of the individuals charged were physicians.

Nutritional Supplement. *See* Dietary Supplement.

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O

Observational Study. Studies in human beings in which biomedical and/or health outcomes are assessed in pre-defined groups of individuals. Subjects in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to the subjects of the study.

Observational Study Model. Primary strategy for subject identification and follow-up.

- **Cohort**: group of individuals, initially defined and composed, with common characteristics (e.g., condition, birth year), who are examined or traced over a given time period
- **Case-control**: group of individuals with specific characteristics (e.g., conditions or exposures) compared to group(s) with different characteristics, but otherwise similar
- **Case-only**: single group of individuals with specific characteristics

- **Case-crossover**: characteristics of case immediately prior to disease onset (sometimes called the hazard period) compared to characteristics of same case at a prior time (i.e., control period)

- **Ecologic or community studies**: geographically defined populations, such as countries or regions within a country, compared on a variety of environmental (e.g., air pollution intensity, hours of sunlight) and/or global measures not reducible to individual level characteristics (e.g., health care system, laws or policies median income, average fat intake, disease rate)
- **Family-based**: studies conducted among family members, such as genetic studies within families or twin studies and studies of family environment

Observational Study Time Perspective. Temporal relationship of observation period to time of subject enrollment.

- **Prospective**: look forward using periodic observations collected predominantly following subject enrollment
- **Retrospective**: look back using observations collected predominantly prior to subject selection and enrollment
- **Cross-sectional**: observations or measurements made at a single point in time, usually at subject enrollment

Obtaining Identifiable Private Information Or Specimens. Means receiving or accessing identifiable private information or identifiable specimens for research purposes. Obtaining includes an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

Off-Site Research. Designates research conducted at study sites that are not part of UT Southwestern Medical Center. Off-site locations may make arrangements to allow the UT Southwestern IRB to act as the reviewing IRB for research conducted at that location or the research may be reviewed by another IRB. Some institutions rely on UT Southwestern IRB to review all research covered by the institution's Federalwide

Assurance. These Affiliated Institution are covered by an IRB Authorization Agreement (IAA) and a Memorandum of Understanding or Agreement (MOU/MOA) with UT Southwestern Medical Center.

Other off-site research may involve researchers from other (non-affiliated) institutions that may or may not already have an FWA/IRB or may involve individual investigators who either are not employed by an institution (Collaborating Individual Investigator) or is employed by an institution that does not routinely conduct research and does not have an FWA/IRB (Collaborating Institutional Investigator).

Office of Human Research Protections (OHRP). Is responsible for implementing HHS regulations governing Research with human subjects. DHHS elevated the Office for Protection from Research Risks (OPRR) to become the Office of Human Research Protections (OHRP) within OPHS, DHHS.

Open-Label Study. In an open label study subjects are assigned to one treatment only. In an open label study two doses of a drug are often compared.

Operator Of Data Center/Repository. Individuals responsible for the operation of the repository and /or data management center. Generally, one individual has overall authority and responsibility for the repository (Principal Investigator). Depending on the structure and use of the repository, a data manager or specimen repository manager is appointed to oversee the operations of the repository. The manager is often the only member of the repository team who has access to the identifying information linked to the data/specimens (all other team members have access only to coded data/specimens).

Oral (verbal) consent. A spoken presentation of the elements of informed consent to the prospective subject or their legally authorized representative. The presentation may be based on information contained within an oral consent script or the written consent

document. Oral consent is often associated with waiving the documentation of consent. Oral consent is usually recorded in the research project files.

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Parent. A child's biological or adoptive mother or biological or adoptive father.

Participation Complete. *See* Subject Status.

Pediatric Research Equity Act (PREA). PREA is designed to address the lack of pediatric use information in drug product labeling.

Permission. Is defined as the agreement of parent(s) or guardian to the participation of their child or ward in research or clinical investigation and includes the elements of consent set forth in federal regulations and outlined in the informed consent template included in the IRB expedited and full review applications.

Pilot testing. "A small scale-study conducted prior to conducting an actual experiment; designed to test and refine procedures." The federal regulations indicate that pilot testing meets the definition of research involving human subjects and requires IRB review.

Examples:

1. Checking to see if the designed tool works
2. Asking people to complete a survey to find out whether a question results in the requested information

3. Testing the intervention with four people before trying it with 60 people

4. Asking people to complete your survey and then revising the questions based on their responses
5. Revising the study after analyzing preliminary data and determining that the data do not address their research question
6. Student researcher designs questionnaire for their study's target population, asks the population to try out the questionnaire, and the questions are revised based on the responses

Planned Emergency Research. Research involving human subjects who are in need of emergency medical intervention (e.g., comparison of methods for providing cardiopulmonary resuscitation), but who cannot give informed consent because of their life-threatening medical conditions and who do not have an available legally authorized representative to provide consent.

Policy. Formal statement of principles on which action(s) for a specific issue are based.

Premarket Approval Application (PMA). The Food and Drug Administration (FDA) process of scientific and regulatory review to evaluation the safety and effectiveness of Class III medical devices (those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury). PMA is the most stringent type of device marketing application required by the FDA, and the applicant must receive FDA approval of the PMA application prior to marketing the device.

Pre-review. The process performed by ORRP staff to determine that a submission for IRB review is complete, including the required materials, copies, and signatures, and that institutional requirements, such as completion of human subjects' protection education and conflict of interest disclosure, have been met.

Pregnancy. Encompasses the time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus.

Principal Investigator. The individual with primary responsibility for the design and conduct of a research project. In multi-center Research, the *Study PI* is the individual with primary responsibility for the entire project and the *Local PI* is the individual with primary responsibility for the research activities under the purview of the UT Southwestern IRB.

The Local PI may be a UT Southwestern employee, student, or agent (e.g., affiliated faculty) or the PI may be an employee or agent of any institution affiliated with the UT Southwestern IRB through a current IRB Authorization Agreement or Memorandum of Understanding/Agreement. The type of relationship an individual has with UT Southwestern determines whether they may serve independently as a PI on their own protocol or if a Faculty Sponsor is required.

The Local PI may designate a Co-Investigator to assist with local PI responsibilities (e.g., report unanticipated problems, authorize modifications or progress reports). The primary responsibility for the conduct of the research may not be assigned to the Co-I.

For FDA regulated research filling a Form FDA 1572, Statement of Investigator, the local PI is the individual listed in Section 1 (investigator).

Prisoner. Means 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.

Prisoner of War: any person captured, detained, held or otherwise under the control of Department of Defense personnel (military or civilian, or contractor employee). Such persons include: Enemy prisoners, civilian internees, retained persons, and lawful and unlawful enemy combatants. Such persons do not include Department of Defense personnel being held for law enforcement purposes.

Privacy. Control over the extent, timing and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Privacy versus confidentiality. Privacy is about people and their choice to share personal information. It is a right in health care and research. Confidentiality is about data. It is the investigator's obligation to protect subjects' information.

Private Information. *Pre-2018 Common Rule Definition:* Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, 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 for obtaining the information to constitute research involving human subjects (bolding added for emphasis).

2018 Common Rule Definition: Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

Procedure or Care. A procedure or activity performed solely for the study.

Program Evaluation. Refers to assessments of the success of established programs in achieving objectives when the assessments are for the use of program managers, for example, a survey to determine if program beneficiaries are aware of the availability of program services or benefits. Not generally considered a research activity as long as the evaluation is designed to assess or improve the program or service rather than to generate knowledge about a disease or condition.

Prospective Studies. Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. These studies need not involve manipulation or intervention, but may be purely observational or involve only the collection of data.

Protected Health Information (PHI). is the term given to health data created, received, stored, or transmitted by HIPAA-covered entities and their business associates in relation to the provision of healthcare, healthcare operations and payment for healthcare services.**Federal Definition:** PHI is Individually Identifiable Health Information transmitted by electronic media, maintained in electronic media, or transmitted or ***maintained in any*** other ***form*** or medium. PHI excludes education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g, records described at 20 U.S.C. 1232g(a)(4)(B)(iv), and employment records held by a covered entity in its role as employer.

The HIPAA definition of Protected Health Information is not meant to include all identifiable information or necessarily to protect identifiers. There is often the misconception that identifiers are removed to protect them from release when in fact they are removed from the health information to protect the individual from anyone knowing the health information that is released is theirs. Many of the actual identifiers are often public domain. The most practical definition is, “any” identifiable information (including demographic information) collected from an individual, that is **created or received by** a health care provider, health plan, employer or health care clearing

house, **and relates to (a) the past, present, or future physical or mental health or condition** of an individual; (b) **the provision of health care to the individual and identifies the individual** or **there is a reasonable basis to believe can be used to identify the individual**."

Note that the identifiable information is further divided into the identifiable information created or received by a health care entity and that identifiable information that is not, plus the requirement that it relate to the health of the patient versus identifiable information that is in no way associated with their health information. Therefore, the collection of health information that is recorded in a manner such that even if someone had the identifiable information they could not tell whose belonged to whom then this may not be considered PHI. An example would be collecting the name and identification number of potential subjects so the research can go into other electronic or paper files and write down (in a physically separate document/media) the health information (without identifiers) but since they do not need to go back later and confirm or check the information there is no need to maintain a link to the identifiers. They are only using the identifiers initially but not recording them with health information.

Alternately it could include identifiable information is further limited to the identifiable information created or received by a health care entity plus the requirement that it relates to the information about who, where, how and when the patient was cared for in the institution which can actually be traced back to the individual.

The concept that this would not be PHI if there was not a reasonable basis for identification can be established if anyone knowledgeable in statistical procedures were to certify that in their opinion subjects could not be identified with the information collected.

Privacy Rule "Safe-Harbor" Identifiers:

The categories of information below are considered identifiers under the privacy rule. Health information accompanied by any of these identifiers is consider PHI and subject to the Privacy Rule.

Data that are stripped of these 18 identifiers (the “safe-harbor” method) are regarded as de-identified, is not PHI and not subject to the Privacy Rule, unless the covered entity has actual knowledge that it would be possible to use the remaining information alone or in combination with other information to identify the subject)

- *Names; Address; Dates except year; Ages over 89 (can be grouped as age 90 or older); Phone numbers; Fax numbers; E-mail addresses; Social security numbers; Medical record numbers; Account numbers; Certificate/license numbers; Health plan beneficiary numbers; Vehicle identifiers and serial numbers, or license plate numbers; Device identifiers and serial numbers; Web Universal Resource Locators (URLs); Internet Protocol (IP) address numbers; Biometric Identifiers, including finger and voice prints; Full face photographic images and any comparable images; Any other unique identifying number, characteristic, or code*

Protocol. The formal design or plan of an experiment or Research activity; specifically, the plan submitted to an IRB for review and to an agency for research support. In some institutions this takes the form of a special template created by the institution. In other institutions who may accept a sponsor’s protocol as partial completion of the requirements for a full protocol additional description of local parameters may be required in the form of addendums or additional forms/sub-forms. In all cases the protocol must contain not only information concerning the larger scale multicenter trial but also address the local context.

Protocol Deviation. See Deviation

Protocol Directed. Includes all procedures, therapies, interventions or interactions that are required by the protocol. Even procedures that are considered to be standard practice are still protocol directed if the protocol requires it.

Protocol Violation. See Violation

Public Service Announcement. A public service announcement is generally a non-profit organization or government broadcast on radio or television, ostensibly for the public good. Public service announcements are intended to modify public attitudes by raising awareness about specific issues.
Although technically it would be difficult to convince a newspaper, radio or television station that information concerning a research study constitutes raising public awareness or was intended for the public good, recruitment advertising activities that must be review by the IRB prior to use include posted notices, paid and unpaid newspaper solicitations or magazine advertisements (which may include public service announcements), websites, radio or television advertisements (which may include public service announcements).

Publicly Available Data. Public data is information that can be freely used, reused and redistributed by anyone with no existing local, national or international legal restrictions on access or usage. Use of publicly available data sets that do not include information that can be used to identify individuals.

"Publicly available" is defined as information shared without conditions on use. This may include data sets that require payment of a fee to gain access to the data.

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Quality Assurance. Refers to activities particular to an institution's QA program, as part of its confidential medical quality-assurance program or other equivalent programs.

Quality Improvement (QI). A process initiated to develop/enhance a practice or procedure and to institutionalize the practice or procedure. A systematic, data-guided activities designed to bring about immediate, positive changes in the delivery of health care in particular settings. QI involves deliberate actions to improve care, guided by data reflecting the effects (e.g., types of practical problem solving; an evidence-based management style; the application of science of how to bring about system change; review of aggregate data at the patient/provider/unit/ organizational level to identify a clinical or management change that can be expected to improve care). QI is generally not considered research – however, QI activities can be research if they are also intended to contribute to generalizable knowledge.

Quorum. The minimal number of members of IRB who must be present at a convened meeting for valid transaction of business.

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Radiation Exposure. In health physics, the quantity used to indicate the amount of ionization in air produced by X-ray or gamma radiation while conducting radiologic procedures.

Radiologic (Radiological) Procedure. Any procedure involving radiation (e.g., X-ray) or a radioactive agent (e.g., radionuclide used in a nuclear medicine study).

Randomization. In randomized controlled studies, the research participants are

assigned by chance, rather than by choice, to either the experimental group or the control group. Randomization reduces bias as much as possible. Randomization is designed to "control" (reduce or eliminate if possible) bias by all means.

Randomized Control Study. A type of scientific experiment - a form of clinical research - most commonly used in testing the safety (or more specifically, information about adverse drug reactions and adverse effects of other treatments) and efficacy or effectiveness of healthcare services (such as medicine or nursing) or health technologies (such as pharmaceuticals, medical devices or surgery). Study subjects, after assessment of eligibility and recruitment, but before the intervention to be studied begins, are randomly allocated to receive one or other of the alternative treatments under study.

Random allocation is complex, but conceptually, the process is like tossing a coin. After randomization, the two (or more) groups of subjects are followed up in exactly the same way, and the only differences between the care they receive, for example, in terms of procedures, tests, outpatient visits, follow-up calls, etc. should be those intrinsic to the treatments being compared. The most important advantage of proper randomization is that it minimizes allocation bias, balancing both known and unknown prognostic factors, in the assignment of treatments."

Recipient Of Data/Specimens. Anyone who receives the data/specimens from the data center/repository. Recipient (sometimes referred to as recipient-investigator) can be from an organization covered by the UT Southwestern IRB or can be from an organization not affiliated UT Southwestern IRB.

Re-consenting. Process of notifying research subjects of changes in the research, including documentation of the subject's continued informed consent through signature on a revised written consent form.

Recorded. Regarding exempt research, “recorded” refers to information (data) that is

"collected" or "documented" during the process of a research investigation. The information may be written, typed, copied, audio or video recorded, etc**.**

Recruitment. A "pre-enrollment" activity used to find potential research participants. It includes identification of potential participants and contacting Individuals to inquire if they are interested in participating in an IRB approved research protocol.

Recruitment activities include:

- reviewing PHI in medical records of Individuals for the purpose of identifying potential candidates for participation in an IRB approved research protocol
- advertisements or solicitations that are intended to be seen or heard by prospective subjects to solicit their participation in a study;
- encounters to discuss the availability of studies and the possibility of entry into a study with a prospective subject;
- dear doctor letters, etc.
- obtaining the results of procedures performed as part of the practice of medicine for the purpose of determining study eligibility (if the IRB approves a waiver of consent and HIPAA waiver).

Once potential subjects are Identified, see Subject Status**-Identified/referred**, an assessment of eligibility (Screening) follows.

Recruiting Methods. Materials, compensation, and other practices or procedures used to inform potential participants about research. *Note: Methods for recruiting research participants are generally distinguished from those of marketing, advertising, or public relations' efforts, which have promoting a product, service, or idea as goals.*

Recruitment Bonus. Payment, merchandise, or other gift or service offered by a sponsor as an incentive or reward to an organization, investigator, or key personnel conducting research designed to accelerate recruitment that is tied to enrollment rate, timing, or numbers.

Recruitment Materials. Announcements; advertisements; flyers; posters; scripts for telephone or other oral communication; letters or email messages; bulletin board tear-offs; Internet postings; newspaper, radio, television, or video broadcasts, or other media used to attract potential participants for research.

Regulatory Binder (Essential Documents). Essential documents are those which individually and collectively permit evaluation of the conduct of a research study and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the regulatory requirements of various federal, state and local agencies.

Regulatory Specialist. Individual who serves as the subject matter expert on institutional policies and federal regulations regarding human subjects' protections.

Regulatory Sponsor. The agency, organization, company or person primarily responsible for *initiating*
and *overseeing* the research and ensuring the study complies with federal regulations

- For clinical trials (studies involving drugs or biologics) this is typically the IND holder, for device studies, this is the IDE holder
- For industry-sponsored trials, typically the pharmaceutical/ device/biotechnology company is the regulatory sponsor
- For non-industry sponsored trials, the regulatory sponsor is typically the PI

Reimbursement. Reimbursement is for expenses and generally requires justification/verification of the expense and should be available to all but may be different for each subject in contrast to Compensation which is usually required to be the same for each subject as payment for participation in Research.

Related Adverse Event Or Probably Related Adverse Event. Means that there is at least a reasonable possibility that the Unexpected Adverse Event may have been caused by the procedures involved in the research. Possibly related should be considered more likely than not, e.g., > 50% chance that it is at least partially related should be the threshold since the alternative would not be considered a reasonable possibility).

Reportable event. An ETHOS process (with an associated form) used by an investigator to report protocol violations (includes noncompliance, serious noncompliance, continuing noncompliance), emergency deviations, Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO), and research-related complaints to the reviewing IRB and/or institutional HRPP.

Repository. Data management centers (data centers) and human specimen repositories (sometimes called registries, banks, or libraries) are used to store data and/or specimens for future use. When the use is for Research purposes, the data centers/repositories must be approved by the Institutional Review Board (IRB). Human Specimen Repositories collect, store, and distribute human tissue/specimen materials for research purposes. Repository activities involve three components: (i) the collectors of tissue samples; (ii) the repository storage and data management center; and (iii) the recipient investigators. Human repository repositories may be combined with data management centers.

Links to Additional Definitions Specific to Repositories:

Affiliated Institution, Data Management Centers, Collector Of Data/Specimens,

Operator Of Data Center/Repository, Recipient Of Data/Specimens, Unidentifiable Data/Specimens , Identifiable Data/Specimens.

Research. *Pre-2018 Common Rule Definition:* A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program considered as research for other purposes. For example, some demonstration and service programs may include research activities.

Under **HHS Regulations (46.102)** research is defined as a "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." The general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects. For example, some "demonstration" and "service" programs may include research activities.

Under **FDA Regulations (21 CFR 56.102)** the term "clinical investigation" is synonymous with "research" and is defined as "any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Food, Drug and Cosmetic Act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. Clinical investigations regulated by the FDA under Sections 505(i) and 520(g) of the Act, include investigations of food, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. The term "clinical investigation" does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be

synonymous for purposes of this part.
Research is subject to 21 CFR 50 and 56 when it involves the use of any drug other than the use of an approved drug in the course of medical practice. Research is subject to 21 CFR 50 and 56 when it involves the use of any medical device other than the use of an approved medical device in the course of medical practice.

The Belmont Report provides additional clarification:

"…the term "research' designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective."

Also see Clinical Investigation *for FDA's definition of research.*

2018 Common Rule Definition: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this rule, the following activities are deemed not to be research:

(i) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(ii) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(iii) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(iv) Authorized operational activities (as determined by each agency) in support of

intelligence, homeland security, defense, or other national security missions.

Research Only. A procedure or activity performed solely for the study.

Research Performance Site. Location/site at which human subjects research may be performed because of an understanding of the local research context and appropriate oversight mechanisms that ensure protection of research participants. *Note: A list of approved UT Southwestern research performance sites is available at Research Performance Sites.*

Retrospective Research. The research study involves data or specimens that already exist in their entirety at the time of IRB submission.

Retrospective Studies. Research conducted by reviewing records (i.e., birth and death certificates, medical records, school or employment records) or information about past events elicited through interviews with persons who have, and controls who do not have, a disease under investigation.

Risk. A potential harm. Generally in research, risks of research that a reasonable person, in what the investigator knows or should know to be the subject's position, would be likely to consider significant in deciding whether or not to participate in the Research should be disclosed to the potential subject.

Risks may be physical, social, legal, economic or psychological in nature, and may relate to employability or insurability. In addition, risks may apply to the individual subject or may apply to a broader segment of the society

Risk is usually discussed in terms of two factors probability (chance) and magnitude (severity). In order to minimize the risk, the researcher and the IRB need to assess the chances the risk will occur and how severe that risk can be, then look at the mechanism

or methods built into the research for decreasing both the chance and severity.

For example, risk that a metal object may become a projectile during an MRI procedure. The severity could be high, but if precautions are taken the probability is low.

Additionally, in certain circumstances additional parameters of risk such as permanence and immediacy should be included in the description of risk in research. For example, it may improve a potential subjects understanding of the risk and assist them in deciding whether or not to participate, if for some risks they were told whether the effect might be permanent rather than self-limiting or at least treatable and for some risks the subject should be informed whether they should only expect this effect immediately or whether it might occur after the have left the care of the researcher in which case might they need emergency care.

Routine (Not-for-Cause) Review. An assessment or examination of something (e.g., a practice or procedure) with the possibility or intention of instituting change if necessary.

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Sample. Also: specimen. Human biological material, including solid material (e.g., tissue, organs) body fluid (e.g., blood, urine, saliva, semen, cerebrospinal fluid), and cells.

Screen Failure. Subjects who consented to participate in research but who were disqualified during screening procedures. *See* Subject Status.

Screened Participant. Individuals who are screened to determine eligibility.

Screening. *See* Subject Status

Serious Adverse Drug Experience (SADE). Any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life- threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include (but are not limited to) allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias, or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Serious adverse event (SAE). Is any Adverse Event that:

1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. results in inpatient hospitalization or prolongation of existing hospitalization;
4. results in a persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect; or
6. based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other

outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

(based on OHRP definition)

Serious Disease or Condition. Means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

Serious noncompliance. Any noncompliance that:

- increases risk of harm to subjects; and/or
- adversely affects the rights, safety, or welfare of subjects (any of which may also be an unanticipated problem); and/or
- adversely affects the integrity of the data and research (i.e., substantially compromises the integrity, reliability, or validity of the research)

Severely Debilitating. Diseases or conditions causing major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Short Form consent document. A written document stating that the elements of informed consent required by regulation have been presented orally to the subject or the subject's legally authorized representative. The short form consent document must be written in a language understandable to the subject or the subject's legally authorized

representative.

Significant Risk (SR) Device. A Significant Risk device is defined [21 CFR 812.3(m)] as a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or
(4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Note: *A significant risk device requires submission to the FDA for an Investigational Device Exemption (IDE) in contrast to a nonsignificant risk device which may be approved by the IRB under FDA Abbreviated Requirements.*

The IRB does not make a SR/NSR device determination when considering requests to approve the use of a Humanitarian Use Device Humanitarian Use Device (HUD) under an FDA approved Humanitarian Device Exemption (HDE).

Single Masked Design. In a single masked design, the subject does not know the treatment assignment but the investigator does.

Source Document. Sometimes referred to as source data, all information in original records of clinical findings, observations, or other activities in a study necessary for the reconstruction and support of the progress and adjudication of outcomes described in the research design. Source data are the first recording of subject-related information. In a drug study, for example, an investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual. Source documents must be complete, accurate, and valid.

Sponsor. Sponsors are the agencies, institutions, companies, organizations,

foundations, or individual grantors responsible for the initiation, management, or financing of a research study. The term sponsor is understood to include any intermediaries, such as contract research organizations or coordinating centers, acting as agents of the sponsor in carrying out the responsibilities above. All research falling under these types of agreements is considered sponsored research.

In FDA regulated research, the Sponsor is the entity who takes responsibility for and initiates a clinical investigation. The sponsor can be any legal entity, including a company, an academic organization, or an individual. The intent of the sponsor's IND/IDE is to allow testing for marketing approval of the drug or device. These are generally considered commercial or corporate IND/IDEs.

Note: the sponsor is often but not always the entity that funds the clinical research – i.e., Financial Sponsor

Sponsor-Investigator. A sponsor-investigator is an individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug/device is being administered, used or dispensed. For administrative reasons, only one individual should be designated as the sponsor.

Usually, the intent of the sponsor-investigator IND/IDE is to gain scientific knowledge without seeking market approval for the drug or device. These are considered 'Investigator-Initiated' or sponsor- investigator IND/IDEs.

Sponsor-Investigator INDs/IDE's. There a three general categories of sponsor-investigator INDs/IDEs:

1) new drug/device developed by the investigator,

2) new uses, new routes of administration, new dosages, or new patient

populations for currently approved drugs, or

3) new use of a significant risk device that has either been cleared under 510 (k) or approved under a Premarket Approval (PMA).

Also known as Investigator Initiated.

Standard Care or Practice. Care or procedures that are routinely or typically provided absent a research study (or generally accepted practice, routine or conventional care). Is a medical or psychological treatment guideline, and can be general or specific. It specifies appropriate treatment based on scientific evidence and collaboration between medical and/or psychological professionals involved in the treatment of a given condition. Some common examples include: treatment standards applied within public hospitals to ensure that all patients receive appropriate care regardless of financial means; or treatment standards for gender identity disorders.

Stipulations (s). Express IRB provisions that must be satisfactorily addressed *before* a human subject research project can be approved and any involvement of human subjects in the research may begin. Under no circumstances do stipulations constitute contingent approval of the research project—approval is neither given nor implied until the PI has received written notice of IRB approval.

Study expiration. If IRB approval of a specific study expires before continuing review and approval occur, investigators must stop all research activities involving human subjects related to that study except where they judge that it is in the best interests of already enrolled subjects to continue to participate.
When investigators make this judgment, they must promptly notify the IRB. When the IRB reviews the investigator's decision, it may decide whether it is in the best interests of already-enrolled subjects to continue to participate in the research by considering the best interests of subjects either one at a time or as a group. If an IRB determines that it

is not in the best interests of already-enrolled subjects to continue to participate, investigators must stop all human subjects research activities, including intervening or interacting with subjects, or obtaining or analyzing identifiable private information about human subjects. Investigators may resume the human subjects research activity once continuing review and approval by the IRB has occurred.

Study Operations Center. Most multi-center studies designate an operations center (generally the lead Principal Investigator (PI)'s location). Study operations centers are designed to assist the study PI in meeting the oversight responsibility of the entire project. Examples of operation center responsibilities include: collection of data and specimens from satellite sites, monitoring safety data, communicating study-wide amendments, regulatory oversight, etc.

In order to meet these responsibilities, most operations centers obtain private, identifiable information from the satellite sites. This action alone constitutes human research requiring IRB approval.

Sub-Investigator. Any investigator who is not the Principal Investigator.

Also, Sub-I.

Subject Status. Used to track the various states (milestones) in a subject's trajectory through a specific research study. UT Southwestern's Clinical Trial Management System (CTMS) developed the following statuses for use in all types of clinical research (not just clinical trials):

- **Identified/Referred -**during recruitment, and individual is identified as a prospective subject: 1) by obtaining the results of procedures performed as part of the practice of medicine (reviewing medical records with an IRB waiver), 2) by responding to recruitment activities, or referred by a provider.
- **Consent Refused**- an identified subject has declined to sign consent for study.
- **Consent Signed**- identified subjects who have been appropriately consented and are awaiting screening to begin.
- **Pre-Screen -**a consented subject who undergoes minimal procedures or gives authorization to obtain additional health records prior to a complete screening

activity. The information obtained in prescreening is used to determine if a subject meets the minimum requirements to proceed to be screened. Consented subjects that are pre-screened are either eligible or ineligible. Eligible participants that pre-screen continue on to screening. Ineligible participants are considered a pre-screen failure.

- **Pre-Screen Failure**-a pre-screened participant determined to be ineligible to proceed to screening as the subject does not meet the minimum eligibility requirements for the study.
- **Screening/Eligibility**-A 'pre-enrollment' activity used to determine eligibility. Screening procedures are necessary solely for the purpose of determining eligibility (including fasting, withdrawal of medication), as a result informed consent must be obtained in some form (i.e., verbal, abbreviated or full informed consent). Prospective subjects that are screened are considered Screened Participant. Screened participants either: eligible or ineligible. Eligible subjects that consent to continue are considered enrolled. Ineligible subjects are considered Screen Failure.
- **Eligible/Screen Successful**- Participant has met all criteria and is eligible for study.
- **Screen Failure**- A screened participant determined to be ineligible for enrollment because they do not meet the eligibility criteria, or whatever other requirements must be met for research participation.
- **Re-screening**- A subject that has previously completed screening and either did not complete the screening process or was determined to be ineligible. If previously arranged (by sponsor or PI) and approved (by IRB), subject can be reentered into the screening process a second time. The

Re-Screening status is appropriate if the sponsor (or PI) wants the re-screening recorded under the same subject ID. If a new subject ID is assigned, the original subject ID status is changed to **Screen Failure.** Re-Screened participants are either: eligible or ineligible. Eligible subjects that consent to continue are considered Enrolled. Ineligible subjects are considered Screen Failure.

- **Enrolled** - Screened participants are enrolled if eligibility is verified (meet all inclusion criteria and none of the exclusion) and they consent to continue in the study.
- **Re-Consent** - Participant re-consented due to modifications to consent forms or upon reaching adult age.
- **Re-Enrolled**- Participant was previously enrolled or accrued to study, was taken off study, and was then re-enrolled.
- **Active Observations** - Applicable to non-interventional studies (e.g., Observational Study, indicates subject is actively involved with study Intervention(s) or Interaction(s).
- **Run In/Wash Out -** Applicable to Interventional Study, indicates a pre-intervention step commonly involving a run-in or wash out of study interventions.
- **Active Treatment/On Treatment** - Applicable to Interventional Study, indicates subject is actively involved with study Intervention(s) (Including the intervention of being tested or evaluated) and/or data collection as per protocol calendar. Status date reflects start of intervention. .
- **Active** – No Research Review - Participant is still 'Active/On Treatment' on a study, but all billable charges are considered routine care (Standard of Care (SoC)) and are paid by insurance – Q1 Modifier. (This status should only be used when there are no research related visits that won't need modifiers to be used on the bill).
- **Off Treatment** - Participant was enrolled on study but is currently not undergoing

any intervention. It differs from “In Follow-up” because the Participant may be scheduled to return to treatment later in the study.

- **Follow-Up As Planned** - Applicable to Interventional Study, indicates the subject has completed the intervention being tested or evaluated as planned and is continuing with non-interventional procedures or other study Interaction(s). It differs from Off Treatment since there is no plan for the Participant to resume any study-related treatment on this study.
- **In Follow-Up – No Research Review-** Participant has completed all study-related interventions/procedures on study and any potential billable charges are considered routine care (Standard of Care (SoC)) and paid by insurance – Q1 Modifier. (This status should only be used when there are no research related visits that won’t need modifiers to be used on the bill).
- **Intervention Stopped Early - following** - applicable to Interventional Study indicates the intervention being tested or evaluated was stopped pre-maturely and the subject is continuing with non-interventional procedures or other study Interaction.
- **Intervention Stopped Early - following-up complete**- applicable to Interventional Study indicates intervention being tested or evaluated was stopped prematurely, the follow-up procedures have been completed.
- **Off Study** - Participant is no longer participating in a study.
- **Transferred** - Participant has been transferred to/from another study site. Enter site information in the notes section. Once ‘transferred’, must appropriately choose proper status within 24 hours.
- **Added in Error** - Participant was added in error and has been removed
- **Withdrawn** - (prior to active, during active, during follow-up) - an early end to all participation for an enrolled subject (even if the subject did not start the treatment).

- **Completed** - indicates that all study procedures (including Intervention), research related Interaction with the subject, and acquiring the subject's Private Identifiable Information were completed as planned. The subject is no longer participating in the research.

Substantive Changes Or Clarifications. Any change or request for additional information required by the IRB to an application (initial, progress report or amendment) that are directly relevant to the determinations required by the IRB under HHS regulations at 45 CFR 46.111.

Summary Document. A written version of the full information presented to a subject or the subject's legally authorized representative during the informed consent process, used in conjunction with a short form consent document. For non-English speaking individuals, the IRB-approved English language consent form may serve as the summary when an appropriately translated document is not available.

Supplement. *See* Dietary Supplement.

Surrogate Consent. When Informed Consent is obtained from someone other than the participant such as with family member consent (parental consent for a minor, immediate family consent during an emergency, etc.) or Legally Authorized Representative (LAR) consent. It is not always required that Informed Consent to participate in research be given by the Legally Authorized Representative (LAR) if another form of surrogate consent is available depending on applicable state law, institutional policy and the determination of the IRB.

See 3.2 INFORMED CONSENT BY SURROGATE for specific information on who may serve as a legally authorized representative or surrogate.

Survey Studies. Whenever you gather information from your constituents or the general public, you need to give some thought to why you are collecting the information and how you plan to use it. Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

Suspension of Research. A suspension of IRB approved research that is required by the IRB, HRPP Director, IRB Chair or designee, or Institutional Official results in a temporary cessation of some or all of the research activities. Research may be suspended: 1) if it is not being conducted in accordance with the IRB approval; 2) when the continuation of the research may adversely affect the rights and welfare of research subjects; or 3) when continuation may represent an immediate threat of harm to the subjects.

Note: a Cessation of some or all research activities Halt voluntarily initiated by the Principal Investigator or sponsor is not considered suspension of research.

Systematic Investigation. Use of a clear plan, system or method to conduct a detailed examination or inquiry for facts.

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Tabled. An IRB “action” that indicates that review was not initiated or was not completed, resulting in postponement of IRB review, usually due to loss of quorum or other administrative issue. Research tabled at a convened meeting will be reviewed at a future convened meeting.

Termination of Research. A termination of IRB approval required by the IRB that

results in a permanent cessation of all research activity. Research may be terminated: 1) if it is not being conducted in accordance with the IRB approval; 2) when the continuation of the research may adversely affect the rights and welfare of research subjects; or 3) when continuation may represent an immediate threat of harm to the subjects.

Note: Cessation of all research activities resulting from the PI's decision to inactivate the study is not considered termination of research. Withdrawal of institutional support for research that results in cessation of all research activities is not considered termination of research.

Test Article. A general term that encompasses Drug, Device, food additives, etc. that are **regulated** by the **FDA**. A test article is any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Public Health Service Act sections 351 and 354-360 F or the Federal Food, Drug, and Cosmetic Act.

Therapeutic Research. Refers to interventions that are designed to determine the efficacy and safety of a therapeutic or diagnostic method. The interventions are not applied solely to enhance the well-being of the individual subject who is sick (note use of the term "subject" as opposed to "patient").
Achievement of maximum possible therapeutic benefit cannot, therefore, be presumed, since the intervention is still being evaluated. The objective of therapeutic Research is to increase generalized knowledge (i.e., test a hypothesis and draw conclusion), and at the same time provide the subject with a needed health benefit. Accordingly, the responsibilities of a physician who is also an investigator must take into consideration the fact that the patient is also a research subject.

Therapeutic Intent. The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinking of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily

be effected). This term is sometimes associated with Phase I drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition, as well as assessing the safety and pharmacology of a drug.

Therapy. Refers to interventions that are applied solely to enhance the well-being of an individual patient who is sick. The interventions are procedures commonly accepted by the medical community and represent standard care.

Transitional Device. A device subject to section 520(l) of the Food, Drug, and Cosmetic Act; a device that FDA considered to be a new drug or an antibiotic drug before May 28, 1976.

Treatment. Interventions designed solely to enhance the well-being of a particular individual.

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

Treatment investigational new drug (IND). A mechanism through the FDA for providing eligible participants with investigational drugs for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.

Treatment Team. Refers to healthcare providers (e.g., physicians, nurses, aides, technicians, and administrative assistants that are normally involved with the delivery of routine medical care.

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Unanticipated adverse device effect (UADE). Is defined by the FDA (21 CFR 812.3(s)). Any serious adverse **effect** on health or safety, **or** any life-threatening **problem or death** caused by (or associated with) a device, **if that effect, problem, or death** was not previously identified in nature, severity, **or** degree of incidence in the investigational plan **or** application; any other unanticipated, serious problem associated with a device that relates to the **rights, safety, or welfare** of subjects.

Unanticipated problems involving risks to subjects or others (UPIRSO). Any events, incidents, experiences, or outcomes that meet **ALL three (3)** of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved protocol, investigator's brochure, and informed consent document; and (b) the characteristics of the subject population being studied;
2. probably or definitely related related to participation in the research; and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic/financial, legal, or social harm) than was previously known or recognized.

UPIRSOs require changes to the research documents or investigational plan (e.g., protocol, IB, and/or informed consent document/process) or corrective actions to protect the rights, safety, or welfare of subjects or others (e.g., notifying subjects of a breach). Therefore, if no changes to the research or corrective actions are made as a result of the event, it is probably **NOT** a UPIRSO.

Unapproved Medical Device. An unapproved medical device is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for premarket approval under section 515 of the Federal Food, Drug, and Cosmetic Act {21 U.S.C. 360(e)}. An unapproved device may be used in

human subjects only if it is approved for clinical testing under an

approved application for an Investigational Device Exemption (IDE) under section 520(g) of the Act {21
U.S.C. 360(j)(g)} and 21 CFR part 812. Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices which require an
IDE. http://www.fda.gov/oc/ohrt/IRBS/devices.html

Undue Influence. Belmont Report states that undue influence occurs "through the offer of Inducements excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance" (National Commission, 1978, p.8). It also argues that "unjustifiable pressures" occur when "persons in positions of authority … urge a course of action for a subject." This includes manipulating a prospective subject's choice by utilizing the "influence of a close relative." Lastly issues may be raised as potential undue influence when judgment may be compromised by financial incentives especially when the subject is not the recipient of the financial incentive. Undue influence needs to be distinguished from coercion for the purposes of UT Southwestern IRB applications of policy. Coercion is considered the use of a threat of harm or punishment to influence behavior; e.g., in general, payments do not constitute coercion per se. There are also less apparent examples of vulnerability to undue influence such as **Institutional vulnerability** and **Deferential vulnerability** to undue influence. **Institutional** is when an individual is subject to the formal authority of others which could influence the subject's participation. Examples- prisoners, military personnel, students, employees. **Deferential** is similar to institutional but arises from informal relationships characterized by inequities in social status (gender, race, class) power or knowledge (doctor-patient relationship), or cognitive ability (elderly person defer to adult kids). Heightened concern that subject's decision re: participation not truly voluntary. Deferential vulnerability can be very subtle- investigators must be especially sensitive to potential for subjects to believe refusing to participate will negative impact their future treatment. Investigators need to be sensitive to such deference and assess whether subject is truly exercising his/her autonomy and

adjust the informed consent accordingly (a suggested addition to the usual consent process might include discussing participation in absence of the individual to whom the potential subject ordinarily defers- additional because the PI or investigator with the relationship may be the best person to discuss the study and answer questions and it would not be appropriate to bypass them all together). Deferential may be misconstrued to include therapeutic misconception but it is generally a separate concept though still requiring consideration in the consent process. Where potential subjects may be drawn to research because of lack of effective standard treatments and desire to find treatment they may be prone to misunderstand the risks and potential benefits and have unreasonable expectations about potential benefits. Pay special attention to ensuring potential benefits of participation are properly characterized. Where investigator is also treating physician, in addition to the issue of deference, there exists a higher risk of therapeutic misconception. Again you may want to consider having impartial third party obtain consent or finalize the consent process in the absence of the individual to whom the potential subject ordinarily defers.

Unexpected Adverse Drug Experience/Reaction (UADR). Any adverse drug experience that is not listed in the current labeling for the drug product. This includes events that may be symptomatically and patho- physiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labeling only listed cerebral vascular accidents. “Unexpected,” as used in this definition, refers to an adverse drug experience that has not been previously observed (i.e. included in the labeling) rather than

from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

Unexpected adverse event. Any adverse event in which the nature, severity, or frequency is not consistent with either:

(1) the known or foreseeable risks of adverse events associated with the procedures involved in the research that are described in (a) the research-related documents, such as the IRB-approved protocol, any applicable investigator's brochure, or the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts;

or

(2) the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event

Unidentifiable. sometimes referred to as "anonymous", are an unidentified collection of human biological materials or data.

or

Unlinked – sometimes referred to as "anonymized", originate from identified human biological materials or data but have been stripped by the source (not the researcher) of all identifiers (including the 18 HIPAA identifiers) or codes such that the ability to identify particular individuals via clinical or demographic information supplied with the sample, or information derived from the Research would be impossible for the investigator, the repository, or a third party.

Unrelated. Unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question.

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Viable. As it pertains to the fetus, means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. Once a fetus is viable it is a premature infant.

Violation. Includes departures (generally intentional on the part of the investigator) from the approved study protocol without prior IRB approval that 1) have the potential to cause harm or increase the risk of harm to one or more research participants; 2) have the potential to damage the scientific integrity of the data collected for the study; or 3) impact a subject's rights, safety, or welfare.

Voluntariness. Is a legal and philosophical concept referring to a choice being made of a person's free will, as opposed to being made as the result of coercion or duress. i.e The participation in the clinical study rests on the concept of the voluntary consent of the individual.

Voluntary. Free of coercion, duress or undue inducement; used in Research context to refer to a subject's decision to participate (or to continue to participate) in a Research activity\

Vulnerable populations in research. Vulnerable populations may include (but are not

limited to): individuals who are pregnant; prisoners; individuals who have been involuntarily committed to a medical facility; children; subordinates such as students, trainees and employees; individuals who are economically or educationally disadvantaged; individuals who have a language barrier; individuals with a cognitive disability; and individuals with an illness for which all standard treatment options have been exhausted. Federal regulations state that "when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects." 45 CFR 46.111(b) FDA regulations expressly identify "mentally disabled persons" as a vulnerable category of subjects in clinical investigations for which IRBs may need to assume increased responsibilities. 21 CFR 56.107(a) and 56.111(b).

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Ward. A child who is placed in the legal custody of the state or other agency, institution or entity, consistent with applicable federal, state or local law.

Withdrawn. Subjects who signed the consent form, but later withdrew from the study, either before or after receiving a study drug, device or intervention. This does not include screen failures. *See* Subject Status*: withdrawn*

Written. *2018 Common Rule Definition:* Or in writing, refers to writing on a tangible medium (e.g., paper) or in an electronic format.

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Z

Revision And Review History

a. June 2026; HRPP; Reference to eIRB updated to ETHOS
b. November 2021; HRPP; Updated minimal risk definition to include examples from DoD definition of minimal risk
c. June 2021; HRPP; Updated the following definitions: Emergency deviation; Deviation (new definition, no longer directs to Noncompliance); • Minor or Administrative Deviations (directs to Deviation); Protocol Violation (directs to Violation); Violation (new definition, no longer directs to Noncompliance) added Protocol; Deviation (directs to Deviation)