**Adjuvant Therapy** – Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.

**Adults with Impaired Decision-making Capacity** – See Cognitively Impaired

**Adverse Event** – An undesirable, unintended and not necessarily unexpected result of therapy or other intervention (e.g., a headache following a spinal tap or intestinal bleeding associated with aspirin therapy).

**Affidavit of Accuracy** – a document signed by a qualified translator in which the translator who performed or verified the translation affirms that the entire document has been translated, that nothing has been omitted or added, and that the translation is true and correct. A qualified translator is an officer or employee of an official translation bureau or agency or a professor or instructor who is teaching the translated language in an accredited college or university in the United States. The type of course being taught must be included in the Affidavit of Accuracy, which must be on official school stationery and notarized.

**Allegation of Non-compliance** - A report of non-compliance that represents an unproven assertion.

**Alternate** - a person, appointed to the IRB by the EVPR, with similar qualifications who is authorized to fill the position, exercise the same duties, authority, responsibility, etc., of an IRB member who is temporarily absent.

**Arm** - Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more.

**Assent** - Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.

**Assurance** – A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved.

**Authorized Institutional Official** - An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.

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

**Belmont Report** - A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

**Beneficence** - An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

**Benefit** - A valued or desired outcome; an advantage.

**Biologic** - Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries. A biological or related product, regulated by the FDA, including blood, vaccines, allergens, tissues, and cellular and gene therapies. Biologics, in contrast to drugs that are chemically synthesized, are derived from living sources (such as humans, animals, and microorganisms). Studies of unlicensed
biologics are regulated according to the IND regulations, except in some cases when the biologic is in a combination product with a medical device. FDA regulates biologics general use and licensing under 21 CFR 600 and 601. (42 U.S.C 262 of the Public Health Service Act.

**Blinded** – A clinical trial is "Blinded" if participants are unaware of whether they are in the experimental or control arm of the study; also called masked.

**Certificate of Confidentiality** – a document issued by the National Institutes of Health (NIH) (or other Federal Agency who may fund research) to protect the privacy of research subjects by protecting investigators and institutions from being compelled in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level to release information that could be used to identify subjects in a research project.

**Chair** – Chair, Co-Chair, or Vice-Chair, as designated on IRB roster submitted to OHRP, unless otherwise indicated. The person who runs the IRB meeting.

**Child** – In Kentucky, all research individuals less than 18 years of age unless the individual is legally emancipated, as these are the individuals who under Kentucky law meet the federal definition of a child. **Children** – Plural of child.

**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), 507(d), or 520(g) of the 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. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies.

**Clinical Trial** - The NIH defines a clinical trial as a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Behavioral human subjects research involving an intervention to modify behavior (diet, physical activity, cognitive therapy, etc.) fits this definition of a clinical trial. Human subjects research to develop or evaluate clinical laboratory tests (e.g. imaging or molecular diagnostic tests) might be considered to be a clinical trial if the test will be used for medical decision making for the subject or the test itself imposes more than minimal risk for subjects. Biomedical clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:

1. **Phase 1** clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., to determine a safe dosage range and to identify side effects).
2. **Phase 2** clinical trials study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.
3. **Phase 3** studies investigate the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.
4. **Phase 4** studies are conducted after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.

There are four possible outcomes from a clinical trial:

1. **Positive trial** – The clinical trial shows that the new treatment has a large beneficial effect and is superior to
standard treatment.
2. Non-inferior trial -- The clinical trial shows that that the new treatment is equivalent to standard treatment. Also called a non-inferiority trial.
3. Inconclusive trial -- The clinical trial shows that the new treatment is neither clearly superior nor clearly inferior to standard treatment.
4. Negative trial -- The clinical trial shows that a new treatment is inferior to standard treatment.

Coded - 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 a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Cognitively Impaired - Having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders, or dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Others, including persons under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interests.

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.

Combination product - A product containing a combination of a drug, a device, or a biological product. Studies of combination products are regulated according to the IND or IDE regulations, depending on the components of the product. The FDA determines which of its organizational components has primary jurisdiction for the premarket review and regulation of products that are comprised of any combination of a drug, device, and/or biological.

Compensation - Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research.

Competence - Technically, a legal term, used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. (See also: Incompetence, Incapacity.)

Confidentiality - Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

Conflict of Interest – an IRB member or consultant/ad hoc reviewer may not vote on a project, and is not counted towards a quorum, when s/he or an immediate family member has a conflict of interest with a project being reviewed, defined as:

- Serving as a co-investigator or other member of the research team; or

- Receiving payments in excess of $10,000 including salary, consulting fees, royalty or licensing payments from intellectual property, honoraria and/or gifts from the study sponsor over the past 12 months or anticipated for the next 12 months (excluding salary and other payments for services
from the University of Louisville); or

- Having equity interest worth more than $10,000 or more than 5% of the business entity as determined by reference to publicly listed prices (excluding mutual funds); or

- Has ownership interest (equity or stock options) of any amount when the value of the interest would be affected by the outcome of the research;

- Has compensation of any amount when the value of the interest would be affected by the outcome of the research;

- Having any equity interest if the value cannot be determined by reference to publicly listed prices (e.g., start-up companies); or

- Holding a position as director, officer, partner, trustee, employee, or any other position of management; or

- Holding patent rights or royalties from such rights whose value may be affected by the outcome of the research, including royalties under any royalty-sharing agreements involving the University of Louisville.

Consent Summary – A summary of the information contained in the complete informed consent document; used with short form consent.

Continuing non-compliance - A pattern of non-compliance that indicates a deficiency likely to result in further non-compliance (e.g., a pattern that indicates lack of attention to or knowledge or understanding about regulations or ethics) or a circumstance in which an investigator fails to cooperate with investigating or correcting non-compliance. Continuing non-compliance includes repeated failures to complete the continuation review process prior to study expiration. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Contract - An agreement; as used here, an agreement that a specific research activity will be performed at the request, and under the direction, of the agency providing the funds. Research performed under contract is more closely controlled by the agency than research performed under a grant.

Contraindicated - Disadvantageous, perhaps dangerous; a treatment that should not be used in certain individuals or conditions due to risks (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).

Controlled Trial - In clinical trials, one group is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo.

Convened meeting – A meeting at which a majority of the members of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. In order for an action to be approved, it shall receive the approval of a majority of those members present at the meeting.

Covered Individual – (Conflict of Interest definition) All University employees. It also includes other individuals with responsibility for the design, performance, or reporting of Institution research, regardless of pay or enrollment status. It also includes individuals conducting research at the University of Louisville, or using University of Louisville researchers,
or using University of Louisville facilities or resources.

**Cross-over Design** - A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy. For example, half of the subjects might be randomly assigned first to the control group and then to the experimental intervention, while the other half would have the sequence reversed.

**Data and Safety Monitoring Board** – committee of scientists, physicians, statisticians, and others that collects and analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

**Debriefing** – Giving subjects previously undisclosed information about the research project following completion of their participation in research. (Note that this usage, which occurs within the behavioral sciences, departs from standard English, in which debriefing is obtaining rather than imparting information.)

**Deception** - in research means that the subject/respondent, at the time of the data collection, is not fully informed of the nature and purpose of the research in which she/he is involved so as to prevent potentially biased reporting of data/information.


**De-Identified Health Information** - De-identified health information neither identifies nor provides a reasonable basis to identify an individual. There are two ways to de-identify information; either: 1) a formal determination by a qualified statistician; or 2) the removal of specified identifiers of the individual and of the individual’s relatives, household members, and employers is required, and is adequate only if the covered entity has no actual knowledge that the remaining information could be used to identify the individual.

**Descriptive Study** - Any study that is not truly experimental (e.g., quasi-experimental studies, correlational studies, record reviews, case histories, and observational studies).

**Diagnostic (Procedure)** - Tests used to identify a disorder or disease in a living person.

**Double-blind Design** - A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-masked."

**Drug** - Any chemical compound that may be used on or administered to humans as an aid in the diagnosis, treatment, cure, mitigation, or prevention of disease or other abnormal conditions.

**Efficacy** – Effectiveness; (Of a drug/treatment) Maximum ability of a drug/treatment to produce a result regardless of dosage.

**Emancipated Child** - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. A legal procedure whereby children become legally responsible for themselves and their parents are no longer responsible financially or otherwise. In Kentucky, a child is considered as emancipated when;
a. he/she becomes self supporting,
b. joins the armed forces,
c. is released from the control and supervision of his or her parents or guardian by the courts, or
d. has a valid marriage.

Pregnancy does not emancipate a female unless other conditions are met. For example, moving out of the parents' or guardian’s house and into an apartment, setting up housekeeping with a partner, and having a baby can be emancipating, because the totality of the circumstances shows an intent to be free of the parents' custody, control, and support. However, the emancipation status will still be determined by the courts and is generally controlled by the contention that the female is free from the supervision and control of her parents or guardian and she has become self supporting, not that she is pregnant.

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 Response - A public health activity undertaken in an urgent or emergency situation, usually because of an identified or suspected imminent health threat to the population, but sometimes because the public and/or government authorities perceive an imminent threat that demands immediate action. The primary purpose of the activity is to document the existence and magnitude of a public health problem in the community and to implement appropriate measures to address the problem.

Emergency use - the use of an FDA-regulated test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

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

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

Ethnographic Research - Ethnography is the study of people and their culture. Ethnographic research, also called fieldwork, involves observation of and interaction with the persons or group being studied in the group's own environment, often for long periods of time.

Evaluation - The systematic application of scientific and statistical procedures for measuring program conceptualization, design, implementation, and utility; making comparisons based on these measurements; and the use of the resulting information to optimize program outcomes.

Excess Human Specimens – remnants of specimens collected for routine clinical care or analysis that would otherwise be discarded. These specimens may also be called “Waste Human Specimens” or “Leftover Human Specimens.”

Existing Data – Data that existed prior to the initiation of a research project.

Expanded Access - Any of the FDA procedures, such as compassionate use, parallel track, and treatment IND that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials. Availability is limited by a risk evaluation and mitigation
(REMS) when the primary purpose is to diagnose, monitor or treat a patient’s disease or condition.

Expeditied Review - Review of proposed research by the IRB chair or a designated voting member or group of voting members rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

Experimental - Term often used to denote a therapy (drug, device, procedure) that is unproven or not yet scientifically validated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study (research) to evaluate its usefulness.

Family member - means any one of the following legally competent persons: Spouse; parents; children (including adopted children); brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

Federal-Wide Assurance (FWA) — An agreement between a federally funded institution and OHRP that stipulates method(s) by which the organization will protect research participants. (66 Fed. Reg. 19139, 19141 (April 13, 2001)).

FDA – Food and Drug Administration, an agency of the federal government established by Congress in 1922 and presently part of the Department of Health and Human Services.

Fetal Material - The placenta, amniotic fluid, fetal membranes, and umbilical cord.

Fetus - The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant [45 CFR 46.203(c)]. The term “fetus” generally refers to later phases of development; the term “embryo” is usually used for earlier phases of development.

Finding of Non-compliance – Non-compliance that is true, or an allegation of non-compliance that is determined to be true based on a preponderance of the evidence.

Fieldwork - Behavioral, social, or anthropological research involving the study of persons or groups in their own environment and without manipulation for research purposes (distinguished from laboratory or controlled settings).

Full-Board Review - Review of proposed research at a convened meeting at which a majority of the membership of the IRB are 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.

Gatekeeper – An individual or organization that controls access to research records, documents or specimens.

Generalizable Knowledge - conclusions, facts, or principles derived from particulars (individual subjects, records, observations, etc.) that are applicable to or affect a whole category (members of a class, kind, or group, a field of knowledge, etc.) and enhance general understanding of a topic.

Gene Therapy - Human gene transfer is the process of transferring genetic material (DNA or RNA) into a person. At present, human gene transfer is experimental and is being studied to see whether it could treat certain health problems by compensating for defective genes, producing a potentially therapeutic substance, or triggering the immune system to fight disease. Human gene transfer may help improve genetic disorders, particularly those conditions that result from inborn errors in a single gene (for example, sickle cell anemia, hemophilia, and cystic fibrosis). It may also hold promise for diseases with more complex origins, like cancer and heart disease. Gene transfer is also being studied as a possible treatment for certain infectious diseases, such as AIDS. This type of experimentation
is sometimes called “gene therapy” research.

**Genetic Screening** - Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.

**Genotype** – The genetic constitution of an individual.

**GINA** - Genetic Information Nondiscrimination Act of 2008 - is a Federal law that prohibits discrimination in health coverage and employment based on genetic information.

**Good Clinical Practice (GCP)** — Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial participants are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible. (International Code of Harmonization for Good Clinical Practice (ICH GCP)). The University of Louisville IRB generally supports the concept of the GCP guidelines but does not mandate that investigators at the university follow all of these guidelines.

**Guardian** - An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

**HIPAA** – Health Insurance Portability and Accountability Act of 1996. HIPAA governs the use and disclosure of protected health information (PHI) that is created or received by a covered entity that relates to:

- the physical or mental health of an individual (living or deceased)
- the provision of health care
- the payment for health care
- identifies the individual or reasonably may be used to identify the individual

Gives individuals the following rights:

- right to request restrictions on use or disclosure of their PHI
- right to access medical records (including research records)
- right to amend medical records
- right to an accounting of disclosure of their PHI
- right to request alternate confidential communications
- right to lodge complaint with covered entity and / or the Department for Health and Human Services

**Administrative Requirements**

- Covered Entity must designate a Privacy Official
- Covered Entity must develop policies and procedures that are HIPAA compliant
- Covered Entity must provide privacy training to the workforce
- Covered Entity must implement administrative, technical and physical safeguards to protect the privacy of PHI
- Covered Entity must develop sanctions for violations of the HIPAA Privacy Rule
- Covered Entity must meet the documentation requirements
to protecting individuals studied in research and that is managed in accordance with these standards and with applicable federal, state and local laws. Some components of the HRPP may be external to the organization seeking accreditation, but the essential components of an HRPP should be identifiable in all cases.

**Human subject** – a living individual about whom an investigator (whether professional or student) conducting research obtains a) data through intervention or interaction with the individual, or b) identifiable private information. Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project.

**Human subject (as defined by the FDA)** - means an individual who is or becomes a participant in research, either as a recipient of the test article as a control or individuals on whose specimens an investigational device is used. A subject may be either a healthy human or a patient. This definition applies to all research involving drugs or devices.

**Humanitarian Device Exemption (HDE)** - A Humanitarian Device Exemption (HDE) is an application that is similar to a pre-market approval (PMA) application, but exempt from the effectiveness requirements of a PMA. An approved HDE authorizes marketing of a Humanitarian Use Device (HUD).

**Humanitarian Use Device (HUD)** - A device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or is manifested in fewer than 4,000 individuals in the United States per year.

**Identifiable personal information** - information relating to a reasonably identifiable person who has a reasonable expectation of privacy, including information about personal characteristics such as culture, age, religion and social status, as well as their life experience and educational, medical or employment histories.

**Incapacity** - Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Often used as a synonym for incompetence.

**Incompetence** - Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity.

**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. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

**Institution** - A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

**Institutional Review Board (IRB)** - any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical or behavioral/social science research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

**Interaction** - includes both physical procedures by which data are gathered (for example, venipuncture) and
Intervention - includes communication or inter-personal contact between investigator and subject.

Investigational Device Exemption (IDE) - Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations.

Investigational New Drug or Device - A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

Investigator - An individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

IRB Committee Member (Member) – An individual appointed by the Executive Vice President for Research or designee to serve on the IRB.

IRB approval - the determination of the IRB that the research study has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

Justice - An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly.

Key Personnel – Participants in a research team who contribute in a substantive way to the scientific development or execution of a project, including the principal investigator. Sometimes called Key Study Personnel (KSP) or Research Team Members (RTMs).

Lapse in IRB Approval – Failure to obtain re-approval of previously approved research prior to the established study expiration date. Lapse in approval is considered noncompliance with federal regulations that may require reporting to regulatory agencies as well as internal reporting to University officials. A second occurrence of lapse in approval is considered continuing noncompliance is will be reported to federal regulatory agencies.

Leftover Human Specimens – remnants of specimens collected for routine clinical care or analysis that would otherwise be discarded. These specimens may also be called “Waste Human Specimens” or “Excess Human Specimens.”

Legally Authorized Representative - An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Longitudinal Study - A study designed to follow subjects forward through time.

Major modifications – Modifications to a research project and/or consent documents that present additional risk to subjects such as dosage escalation, additional procedures or tests, significant increases in time commitment by subject, etc. Substantive protocol revisions also are considered major modifications.

Major Violation - A violation that may impact subject safety, affect the integrity of study data and/or affect subject’s willingness to participate in the study.
Medical Device - A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

Mentally Disabled – See Cognitively impaired.

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 research that involves prisoners, minimal risk is defined as the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons (45 CFR 46.303(d)).

Minor (in reference to a person) – In Kentucky, means any person who has not reached the age of eighteen (18). In the Kentucky Revised Statutes, the definition of a “minor” and a “child” are identical.

Minor - Lesser in seriousness or danger

Minor modifications – Modifications to a research project and/or consent documents that pose no additional risk to subjects such as changes in title, co-investigator (s), funding sources; addition or modification of procedures that fall into one of the categories eligible for expedited review; or modifications that maintain similar or increased safeguards to protect the subject.

Minor Violation - A violation that does not affect subject safety, compromise the integrity of study data and/or affect subject’s willingness to participate in the study.

Monitoring - The act of overseeing the progress of a research study to ensure that the rights and well-being of participants are protected, that the data are accurate, complete and verifiable, and that the conduct of the research is in compliance with the protocol, with applicable regulatory requirements and with standards of the field.

Negligence - Failure to exercise the degree of care considered reasonable under the circumstances, resulting in an unintended injury to another party.

New Drug Application (NDA) - Request for FDA approval to market a new drug.

Non-affiliated Member - Member of an Institutional Review Board who has no ties to the parent institution, its staff, or faculty. This individual is usually from the local community (e.g., minister, business person, attorney, teacher, homemaker).

Non-compliance - Any action or activity associated with the conduct or oversight of research involving human subjects that fails to comply with federal regulations or institutional policies governing such research. Non-compliance actions may range from minor to serious, be unintentional or willful, and may occur once or several times. The degree of non-compliance is evaluated on a case-by-case basis and will take into account such considerations as to what degree subjects were harmed or placed at an increased risk and willfulness of the non-compliance. Examples include, but are not limited to:

1. Failure to obtain IRB approval;
2. Inadequate or non-existent procedures for the informed consent process;
3. Inadequate supervision;
4. Failure to follow recommendations made by the IRB;
5. Failure to report serious adverse events, unanticipated problems, or protocol changes; and
6. Failure to provide ongoing progress reports.

**Non-Identifiable Tissue** - tissue that has been de-identified by the investigator(s) or tissue supplier(s) in preparing the tissue for research requiring no identifiable connection to the donor.

**Non-significant Risk (NSR)** - An NSR device investigation is one that does not meet the definition for a significant risk study. NSR device studies, however, should not be confused with the concept of "minimal risk," a term utilized in the IRB regulations to identify certain studies that may be approved through an "expedited review" procedure.

**Normal Volunteers** - Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.

**Null Hypothesis** - The proposition, to be tested statistically, that the experimental intervention has "no effect," meaning that the treatment and control groups will not differ as a result of the intervention. Investigators usually hope that the data will demonstrate some effect from the intervention, thereby allowing the investigator to reject the null hypothesis.

**Nuremberg Code** - A code of research ethics developed during the trials of Nazi war criminals following World War II and widely adopted as a standard during the 1950s and 1960s for protecting human subjects.

**Off-Label Use** - A drug prescribed for conditions other than those approved by the FDA.

**Office of Human Research Protections (OHRP)** – The Office for Human Research Protections supports, strengthens and provides leadership to the nation’s system for protecting volunteers in research that is conducted or supported by the U.S. Department of Health and Human Services (HHS).

**Open Label Design** - An experimental design in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

**Orphan Drugs** – Drugs and biologics defined as those intended for the safe and effective treatment, diagnosis or prevention or rare diseases/disorders that affect fewer than 200,000 people in the US.

**Paternalism** - Making decisions for others against or apart from their wishes with the intent of doing them good.

**Phase 1, 2, 3, 4 Drug Trials** - Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to post marketing studies (Phase 4).

- **Phase 1 Drug Trial** - Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include...
studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.

- **Phase 2 Drug Trial** - Phase 2 trials include controlled clinical studies conducted to evaluate the drug’s effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well-controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.

- **Phase 3 Drug Trial** - Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide and adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand patient-subjects.

- **Phase 4 Drug Trial** - Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain post-marketing (Phase 4) studies to delineate additional information about the drug’s risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time [21 CFR §312.85].

**Phenotype** - The physical manifestation of a gene function.

**PHS** - Public Health Service. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.

**Placebo** - A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than actual power of a drug.

**Planned Emergency Research** – Planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived (21 CFR 50.24).

**Principal Investigator** - A qualified person who directs a research project or program, may write the protocol, and oversees the scientific, technical and day-to-day management of the research.

**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 (45 CFR 46.303(c)).

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

**Private Information** - 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.

**Program Evaluation** - An essential organizational practice in public health using a systematic approach to improve and account for public health actions.

**Protected Health Information (PHI)** – Individually identifiable health information including demographic data, that relates to:

- the individual’s past, present or future physical or mental health or condition,
- the provision of health care to the individual, or
- the past, present, or future payment for the provision of health care to the individual,
- and that identifies the individual or for which there is a reasonable basis to believe can be used to identify the individual. Individually identifiable health information includes many common identifiers (e.g., name, address, birth date, Social Security Number).

**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. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

**Protocol Deviation** - Any alteration/ modification to the IRB-approved protocol. The protocol includes the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.

**Protocol Exception** - Any temporary protocol deviation that is approved by the IRB prior to its initiation, e.g., enrollment of a subject who does meet the eligibility criteria. Note: Any permanent change to the protocol constitutes an amendment that must be submitted to the IRB for approval prior to initiation.

**Protocol Violation** - Any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

- **Major Violation** - a violation that may impact subject safety, affect the integrity of study data and/or affect subject’s willingness to participate in the study.
- **Minor Violation** - a violation that does not impact subject safety, compromise the integrity of study data and/or affect subject’s willingness to participate in the study.

**Quality Improvement (QI)** - Periodic examination of organizational activities, policies, procedures and performance to identify best practices and target areas in need of improvement; includes implementation of corrective actions or policy changes where needed. In medical institutions, QA/QI is a necessary, integral part of hospital operations and is not subject to review as research, as defined under federal regulation. Rather, it is governed by Joint Commission and hospital standards.
Examples of QA-QI projects that are not human subjects research:

- Data collection for internal departmental, school, hospital, or other University administrative purposes (such as teaching evaluations, customer service surveys, or customer satisfaction surveys).
- Service surveys issued or completed by University or hospital personnel for the intent and purposes of improving services and programs, or for developing new services or programs for students, employees, or alumni, as long as the privacy of the subjects is protected, the confidentiality of individual responses are maintained, and survey participation is voluntary. This would include surveys by professional societies or University consortia.

Quorum – A majority of voting members of an IRB, including at least one member whose primary expertise is in a nonscientific area.

Radioactive Drug - Any substance defined as a drug in §201(b)(1) of the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons [21 CFR 310.3(n)]. Included are any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products," as defined in 21 CFR 600.3(ee). Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.

Randomization - Assignment of subjects to different treatments, interventions, or conditions according to chance rather than systematically (e.g., as dictated by the standard or usual response to their condition, history, or prognosis, or according to demographic characteristics). Random assignment of subjects to conditions is an essential element of experimental research because it makes more likely the probability that differences observed between subject groups are the result of the experimental intervention.

Recombinant DNA Technology - "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.

Recruiting Tools – any printed, video, audio or electronic media used for recruiting of or providing information to subjects or potential subjects in a research project.

Remission - A period in which the signs and symptoms of a disease are diminished or in abeyance. The term "remission" is used when one cannot say with confidence that the disease has been cured.

Research - a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research even if they are a component of a larger non-research activity (e.g., instruction, demonstration).

Retrospective Studies - Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, school records, or employment records) or by obtaining information about past events elicited through interviews or surveys. Case control studies are an example of this type of research.

Risk – the probability of harm or injury (physical, psychological, social, legal, or economic) occurring as a result of participation in a research study. Both the probability and magnitude may vary from minimal to significant.

Sequestration – segregating, holding separate.
Serious adverse experience (SAE) – Any adverse experience associated with the use of the drug/device that results in any of the following outcomes: death, a life-threatening adverse 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 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 above.

Serious Non-compliance - An action or omission in the conduct or oversight of research involving human subjects that affects the rights and welfare of participants, increases risks to participants, decreases potential benefits or compromises the integrity or validity of the research. Examples of serious non-compliance include, but are not limited to:
1. Conducting non-exempt research without IRB approval;
2. Enrollment of subjects that fail to meet the protocol enrollment criteria and increase subject risk;
3. Enrollment of research subjects while study approval has lapsed; or
4. Serious protocol deviations that may place subjects at risk from the research.

Significant Financial Interest - means anything of economic or monetary value that to an independent observer would be or reasonably appear to be affected by research. Please refer to the University of Louisville Policy and Procedures For Oversight of Individual Financial Interests in Research for a more comprehensive definition of significant financial interest.

Significant Risk (SR) Device - An SR device study is defined as a study of 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.

Single-blind Design - Typically, a study design in which the investigator, but not the subject, knows the identity of the treatment assignment. Occasionally the subject, but not the investigator, knows the assignment. Sometimes called "single-masked design."

Site Visit - A visit by agency officials, representatives, or consultants to the location of a research activity to assess the adequacy of IRB protection of human subjects or the capability of personnel to conduct the research.

Sponsor - a person or other entity that initiates a research study, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

Sponsor-investigator - means an individual who both initiates and actually conducts, alone or with others a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., corporation or agency.

Standard Treatment - A treatment currently in wide use and approved by the FDA, considered to be effective in the treatment of a specific disease or condition.

Standard of Care - Treatment regimen or medical management based on state of the art participant care.

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Statistical Significance - A determination of the probability of obtaining the particular distribution of the data on the assumption that the null hypothesis is true. Or, more simply put, the probability of coming to a false positive conclusion.

Surveys - Studies designed to obtain information from a large number of respondents through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

Sub-investigator - The FDA regulations [21 CFR 312.3(b)] specify that in the event an investigation is conducted by a team of individuals, a sub-investigator is any other individual member of the study team.

Substantially Equivalent Language - Language though different, is interpreted to have the same intended meaning. Used in reference when comparing consent form language to executed contract language in areas such as research related injury, expectation of researchers and subjects, subject payment, or other aspects of a human study where a subject is provide information at a language level the subject understands.

Surveillance - The ongoing, systematic collection, analysis, and interpretation of outcome-specific data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease or injury.

Suspension – the temporary closing of a human research project or discontinuing an investigator’s or key personnel’s privilege to conduct or to participate in the conduct of human research at the University of Louisville. The suspension may be partial in that certain activities may continue while others may stop or it may be complete in that no activity related to the human research or related to the privilege to conduct or participate in the conduct of human research may proceed. The IRB will make this determination.

Systematic Investigation - a methodological procedure or plan, carried out in an organized manner, involving testing and evaluation, designed to develop or contribute to generalizable knowledge. A process that entails going from identification and articulation of the scientific or technological obstacles/uncertainties, hypothesis formulation, through testing by experimentation or analysis, to the statement of logical conclusions. A predetermined method for answering certain questions or studying a specific program or topic.

Termination – the permanent closing of all activities related to a human research project or an investigator’s or key personnel’s privilege to conduct or to participate in the conduct of human research at the University of Louisville except the continuation of follow-up activities necessary to protect subject safety.

Test article - means 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 act or under sections 351 and 354-360F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n).

Therapy - Treatment intended and expected to alleviate a disease or disorder.

Unanticipated problem involving risks to subjects or others – unexpected, serious, and would have implications for the conduct of the study, or is unexpected (in terms of nature, severity, or frequency), related or possibly related to participation in the research; and suggests that the research may place subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

For the purposes of this guide unanticipated problem involving risks to subjects or others, UPIRTSO, and unanticipated problem are considered to have the same meaning as described in the definition of Unanticipated problem.
involving risks to subjects or others.

**Undue Influence** - attempting to interfere with the normal functioning and decision-making of the IRB or to influence an IRB member or staff, a PI or any other member of the research team outside of established processes or normal and accepted methods, in order to obtain a particular result, decision or action by the IRB or one of its members or staff.

**Unexpected adverse experience (UAE)** – Any adverse experience associated with the use of the drug/device, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information provided to subjects and the IRB.

**Vaccine** - A biologic product generally made from an infectious agent or its components — a virus, bacterium, or other microorganism — that is killed (inactive) or live-attenuated (active, although weakened). Vaccines may also be biochemically synthesized or made through recombinant DNA techniques.
Vulnerable Subjects/Participants - Individuals who lack the capacity to provide informed consent or whose willingness to participate in research may be unduly influenced by others. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments, and economically or educationally disadvantaged persons. (45CFR 46.111(a)(3); 45CFR 46.111 (b); 45CFR 46 Subparts B, C, and D)

Waste Human Specimen - remnants of specimens collected for routine clinical care or analysis that would otherwise be discarded.

Witness - Impartial, non-involved observer of the consent process for enrollment into a research study.