Issuing Department: Human Subjects Protection Program
Policy Number: 2011-007.0
Policy Title: Definitions Applied to Policies

Purpose

The purpose of this policy is to set forth one document that defines various terms used within other policies issued by the Human Subjects Protection Program. This will reduce redundancy of defining a term in multiple policies and help to ensure consistency in terminology throughout all policies.

Definitions

Administer: The direct application of a drug or device to the body of a patient or research subject by injection, inhalation, ingestion or any other means.

Administrative Review: As related to DoD-supported research, a review of a research protocol and supporting documents (e.g. , safety review, scientific review, IRB minutes) which ensures the institution engaged in the research involving human subjects has met the requirements of all applicable regulations and policies. This is NOT an IRB review.

Adverse Event: Any untoward medical occurrence that presents during the course of a clinical investigation that might be caused by either the condition under study or by the research intervention. Adverse events are categorized into those that are expected (predictable) and those that are unexpected (unpredictable). Adverse events include but are not limited to, adverse reactions to drugs, biologics, radioisotope labeled drugs, and medical devices. An adverse event is considered an unanticipated problem involving risk to subjects or others only when the event is unexpected (see definition below), related or possibly related to the research intervention (see definition below), and places the subjects or others at greater risk of harm than was previously recognized.

Adverse Event – Expected: An event that is anticipated on the basis of prior experience with the drug/device under investigation or with related drugs; an event identified in the Investigator's Brochure and/or study drug labels for post marketing studies; an event that is likely due to the underlying condition of the patient being studied; or an events attributed to the patient population being studied. Such events do not require reporting to the IRB (unless the nature, severity or frequency of the events is different/greater than previously anticipated) but may require reporting to the sponsor based on terms of the clinical trial agreement and /or protocol.

Adverse Event - External: The research participant signed an informed consent form from another institution. These events do not require reporting to the IRB unless the sponsor specifically states that the event is an unanticipated problem that has been reported to the FDA and for which a corrective measure has been implemented by the sponsor.

Adverse Event - Internal: The subject signed a University of Connecticut Health Center informed consent document. Principal investigators should assess all internal adverse events, document their assessment of the event, and report accordingly to the IRB (i.e. if the event is unexpected and related or possibly related to the research intervention and may place subjects are greater risk than previously recognized).

Adverse Event – Life Threatening: Any adverse drug experience that places the patient/subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred (21CFR 312.32).

Adverse Event – Non-serious: Any undesirable symptom or occurrence a subject experiences during participation in a clinical trial that does not meet the serious criteria.

Adverse Event, Related: An internal event is related to the research procedures if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures. The sponsor will make the determination of relatedness for external events.

Adverse Event – Serious: those events that meet at least one of the following criteria:

- Death
- Life-threatening
- Hospitalization/prolongation of existing hospitalization
- Congenital anomaly/birth defect
- Persistent or significant disability/incapacity
- An important medical event that, based upon appropriate medical judgment, requires medical or surgical intervention to prevent one of the outcomes listed above.

  A *non-serious adverse event* is any undesirable symptom or occurrence a subject experiences during participation in a clinical trial that does not meet the criteria for serious.

Adverse Event – Unexpected: Any untoward medical occurrence not listed in the protocol and the informed consent document and not anticipated on the basis of prior experience with the intervention under investigation or with related interventions; an event that cannot be attributed to the underlying condition of the patient being studied or to the patient population; or expected events with frequency and/or severity exceeding what was anticipated.

Agent: An individual performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

Assent: An affirmative agreement to participate in research (e.g. clinical investigation) used with those who are not competent or not of legal age to provide informed consent. Failure to object may not be construed as assent. Assent must be accompanied by consent of a parent or legally authorized representative.

Case Report: Per NCI dictionary of cancer terms, a detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). At UCHC, this definition applies across all clinical disciplines, and single case report does not require prospective review by the IRB.

Case Series: Per NCI dictionary of cancer terms, a group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. At UCHC,

this definition applies across all clinical disciplines and any summary of four or more cases requires prospective review by the IRB.

Causality/Attribution: Both expected and unexpected adverse events are further subdivided by causality into those attributable to the condition or patient population under study and those attributable to the research intervention. Attribution for internal adverse events is the responsibility of the PI. As a disclaimer, assignment of an unexpected adverse event to the research intervention does not necessarily imply agreement as to the cause by the manufacturers, suppliers or the FDA.

Child: See Vulnerable Populations - Children

Classified Information: Information that has been determined pursuant to Executive Order 13526 or any predecessor order to require protection against unauthorized disclosure and is marked to indicate its classified status when in documentary form.

Classified Research: Research where the protocol or other information required by the IRB for review and oversight or required or provided by the research subjects incudes classified information.

Clinical Investigation (21 CFR 312): Any experiment (i.e. any use of a drug except for the use of a marketed drug in the course of medical practice) in which a drug is administered or dispensed to, or used involving, one or more human subjects.

Clinical Investigation (FDA): Any experiment that involves a test article and **one or more** human subjects and that is either 1) subject to requirements for prior submission to the FDA under §505(i) or §520(g); or 2) not subject to the requirements for prior submission to the FDA under those sections but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of 21 CFR 58, Good Laboratory Practice Regulations, regarding non-clinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102 (c))

Clinical Trial (UCHC): A clinical trial is a systematic, organized, prospective intervention study in human subjects that is conducted according to a formal study plan (protocol) and that has measurable efficacy and/or safety-related outcomes that are amenable to statistical analysis. It employs one or more intervention technique(s) including prophylactic, screening, diagnostic, or therapeutic agents, devices, or procedures.

Coercion: The act of bringing about a decision or action by force or threat.

Co-Investigator: Individual working on an approved research project under the direction of the Principal Investigator. Co-investigators are appointed to a study by the PI and must be approved by the IRB. Co-investigator is considered synonymous with sub-investigator.

Conflict of Interest: In conducting or reviewing human subject research, a conflict of interest is defined as a situation in which an individual (or someone in his/her immediate family) has a significant financial, professional or personal, interest in the approval or outcome of a study and the interest could affect decisions related to the design, conduct or reporting of the research; or the review of the research.

Delivery: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

Detainee: Any person captured, detained, held, or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power. A detainee may also include the following categories: Retained Persons, Enemy Combatant; Lawful Enemy Combatant, Unlawful Enemy Combatant Enemy Prisoner of War, Retained Person, Civilian Internee (refer to DoD Directive 2310.0E for detailed definition of each category of detainee.)

Department of Defense (DoD) Personnel: DoD civilian employees and members of the military services.

Device: Instruments, apparatus and contrivances, including their components, parts and accessories, intended (a) for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans or other animals, or (b) to affect the structure or any function of the body of humans or other animals (excluding contact lenses)

Device, Custom: A device 1) necessarily deviates from devices generally available or from an applicable performance standard or premarket 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.

Device, Investigational: A device, including a transitional device, that is the object of an investigation

Device, Investigational Exemption (IDE): An IDE allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. Clinical evaluation of devices that have not been cleared for marketing requires:

- An IDE approved by an institutional review board (IRB). If the study involves a significant risk device, the IDE must also be approved by FDA
- Informed consent from all patients
- Labeling for investigational use only
- Monitoring of the study and
- Required records and reports

An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with other requirements of the Food, Drug, and Cosmetic Act that would apply to devices in commercial distribution. Sponsors need not submit a PMA or Premarket Notification, register their establishment, or list the device while the device is under investigation.

Sponsors of IDE's are also exempt from the Quality System (QS) Regulation except for the requirements for design control.

A sponsor of a significant risk device study must submit a complete IDE application to FDA. There are no preprinted forms for an IDE application; however, an IDE application must include certain required information. The sponsor must demonstrate in the application that there is reason to believe that the risks to human subjects from the proposed investigation are outweighed by the anticipated benefits to subjects and the importance of the knowledge to be gained, that the investigation is scientifically sound, and that there is reason to believe that the device as proposed for use will be effective.

Device, Significant Risk (SR): 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 a 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.

Device, Transitional: A device subject to section 520(l) of the FD&C Act and which FDA previously regulated as a new drug or an antibiotic drug before May 28, 1976

Device, Non-Significant Risk (NSR): A NSR device is one that does not meet the definition of a SR device.

Device, Unanticipated Adverse Device Effect: 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 (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that related to the rights, safety or welfare of subjects. (21 CFR 812)

Disclosure: The release, transfer, provision of access to, or divulging in any other manner of information outside the entity holding the information. (45 CFR 164)

Dispense: Those acts of processing a drug or device for delivery or for administration for a patient pursuant to a prescription consisting of : (a) comparing the direction on the label with the direction on the prescription to determine accuracy; (b) the selection of the drug or device from stock to fill the prescription; (c) the counting, measuring, compounding or preparation of the drug or device; (d) the placing of the drug or device in the proper container; (e) the affixing of the label to the container and; (f) the addition to a written prescription of any required notations. Dispensing does not include the acts of delivering a drug or device to a patient or of administering the drug or device to the patient. (CT Chapter 400j)

Emancipated Child (Emancipated Minor): A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage, or procreation. In CT , must be adjudicated by the court.

Emergency Use: The use of a 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 prior IRB approval.

Exempt: A project that does constitute human subject research but that also falls within one or more of the federally recognized categories that allow for the project to be excused from satisfying regulatory requirements for approval regard human subject protections. The IRB reserves the right to impose additional requirements on exempt research.

Experimental Subject: The Department of Defense defines "Research Involving a Human Being as an Experimental Subject" as an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction (32CFR.210.102 (f) reference (c)). Examples of interventions or interactions include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

External Agencies: Government entities that provide funding and/or have oversight interest in approved research studies, including the Office for Human Research Protections, Food and Drug Administration and other agencies as applicable to specific studies.

Family Member: Any one of the following legally competent persons: spouse; parent; child (including adopted child); brother, sister, and spouse of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

Family Member, Immediate: As related to conflict of interest, the investigator's or IRB member's spouse, or dependent children.

Federalwide Assurance: An agreement between an institution and the Department of Health and Human Services (HHS) through which an institution commits to HHS that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46.

Financial Interest Related to the Research: A financial interest in the sponsor, product or service being tested.

Generalizable Knowledge: Information resulting from a systematic investigation that has at least one of the following characteristics:

- it is intended to be disseminated to a broader external audience by means such as professional publication and/or formal presentation
- it may be applicable to circumstances other than those under which the systematic investigation was conducted

Guardian: Per the common rule a guardian is an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. Per FDA regulations a guardian is 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; or an individual who is authorized to consent on behalf of a child to participation in research.

When research is conducted in Connecticut, the persons who meet the definition of guardian are court-appointed guardians with the authority to consent to major medical, psychiatric or surgical treatment. When research is conducted outside of Connecticut, and review and approval by a local IRB or its equivalent is not required, the investigator must consult with legal counsel as to who can serve as the guardian and submit documentation of legal counsel's opinion.

Health Care Representative: Per Connecticut General Statutes § 19a-570(5) the individual appointed by a declarant pursuant to an appointment of health care representative for the purpose of making health care decisions on behalf of the declarant.

Human Fetal Tissue: Tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.

Human Subject, (per Common Rule)**:** A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual or (2) identifiable private information.

Human Subject, (per FDA)**:** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

Human Subject Research: Any activity that encompasses the definition of human subject and research as set forth by OHRP or human subject and clinical investigation as set forth by the FDA.

Humanitarian Device Exemption: To obtain approval for an humanitarian use device (HUD), an humanitarian device exemption (HDE) application is submitted to FDA. An HDE is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market. An approved HDE authorizes marketing of the HUD.

Humanitarian Use Device: A marketed medical device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individual in the United States per year. The designation of a device as an HUD is made by the FDA under a category of approval known as Humanitarian Device Exemption (HDE). An investigator or a sponsor may submit a request for HUD designation to the FDA. To receive the determination as an HUD, the device must be expected to benefit fewer than 4,000 people in the US per year and no

comparable device, other than another HUD approved under the HDE regulation or a device being studied under an approved Investigational Device Exemption is available to treat or diagnose the condition.

Illiterate: Having little or no education; *especially* unable to read or write

Immediate Family: Spouse, domestic partner, child/stepchild, who stands to gain financially by the employee's decisions. Interest related to the research means an interest in the sponsor of the research or a product or service being tested. For example, if an investigator conducts a non-sponsored study on drug X and the investigator owns stock in the manufacturer of drug X, that interest is considered an interest related to the research.

Immediately Life-threatening Disease or Condition (21 CFR 312.300)**:** 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.

Implant: A device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more. FDA may, in order to protect public health, determine that devices placed in subjects for shorter periods are also "implants' for purposes of 21 CFR 812.

IND (21 CFR 312): Investigational new drug application; often synonymous with "Notice of Claimed Investigational Exemption for a New Drug"

Individually Identifiable Heath Information: Information that is a subset of health information, including demographic information collected from an individual, and is created or received by a heath care provider, health plan, employer or health care clearinghouse and 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 of the provision of health care to an individual, and that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual. (45 CFR 164)

Informed Consent Process: A process that occurs between a potential subject (or their legally authorized representative) and a knowledgeable and authorized member of the research team that provides the prospective research subject (or the subject's legally authorized representative) with information pertaining to the research study and sufficient opportunity to consider whether or not to participate.

Informed Consent Form: The IRB approved form used to document the essence of the discussion between the individual obtaining consent and the potential subject or the subject's legally authorized representative

Institutional Officials: Include the individuals identified in Policy 2002-42, Review and Approval of Research Involving Human Subjects.

Institutional Review Board (IRB): A board established, operating and functioning in accordance with regulatory criteria (e.g. at 45 CFR 46 and 21 CFR 56) and formally designated by an institution to review biomedical and/or social and behavioral research involving subjects.

IRB Approval: The determination of the IRB that the research 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.

Interaction: Includes communication or interpersonal contact between an investigator and a research participant

Intervention: Both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes.

Investigation (21 CFR 812): A clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device

Investigational Device: An investigational device is a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

Investigational New Drug (21 CFR 312): A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. Synonymous with investigational drug.

Investigator (21 CFR 312..305(c)(1))**:** As related to an expanded access use a licensed physician under whose immediate direction an investigational drug is administered or dispensed for an expanded access use**.**

Investigator (21 CFR 812)**:** 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 individual, is the responsible leader of that team

Legally Authorized Representative: Under DHHS and FDA regulations 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.

When research is conducted in Connecticut, the persons who meet the definition of a legally authorized representative are a child's parent(s), court-appointed conservators or guardians, individuals designated as having power of attorney for health care, or individuals designated as health care representatives. Consent from next-of-kin is not acceptable absent one of the prior designations. When research is conducted outside of Connecticut, and review and approval by a local IRB or its equivalent is not required, the investigator must consult with legal counsel as to who can serve as the legally authorized representative and submit documentation of legal counsel's opinion.

Life Threatening: As related to emergency use policies, encompasses both life-threatening and severely debilitating conditions. 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 trail 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**.**

Member, Affiliated: An employee or agent of U. of CT Health Center (or a member of that person's immediate family) is considered affiliated. Affiliated members also include, individuals who are part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; healthcare providers holding credentials to practice at the institution; and volunteers working at the institution on business unrelated to the IRB.

Member, Experienced: An IRB member who has completed the required training and attended at least 6 IRB meetings.

Member, Non-affiliated: An individual that has no affiliation with the organization registering the IRB (i.e. UCHC), other than as an IRB member, is considered unaffiliated. Unaffiliated members may include people whose only association with the institution is that of a patient, subject, or former student at that institution.

Member, Non-Scientific: A member whose training, background, and occupation **would incline** them to view research activities from a standpoint **outside of** any biomedical or behavioral scientific discipline should be considered a nonscientist

Member, Scientific – A member whose training, background, and occupation **would incline** them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline.

Modification, Minor: A minor modification to previously approved research is a change that may be reviewed and approved using the expedited process. Modifications are considered minor changes when they are of an administrative nature, do not substantially change the design of the study, do not pose information pertaining to greater than minimal risks to subjects, and/ or fall into a category or categories of research that could be reviewed using the expedited procedure.

Modification, Full Board: Changes to an approved study that will increase the level of risk to which a subject is exposed or are substantial changes to the procedures or design of a protocol and/or informed consent form as it was previously approved.

Noncompliance: Any action that is taken or occurs that is not in accordance with an IRB approved study, IRB policies or regulations or represents failure to follow the requirements and/or determinations of the IRB. Noncompliance may be minor (e.g. a participant is one day late for visit due to family emergency and there is no impact on the safety of the participant due to the late visit, or a study coordinator schedules a follow-up visit 2 days outside of the study window and there is no impact on the

safety of the subject) or it may be considered serious or continuing. Noncompliance is sometimes referred to as a protocol deviation.

Noncompliance, Continuing: Noncompliance that reflects a pattern of noncompliance that if allowed to continue is likely to increase the risks to subjects, adversely affect the rights and/or welfare of subjects, or affect the scientific integrity of the study. It may involve the same mistake being made repeatedly within one study or across studies (e.g. a co-investigator on two of the PI's approved studies fails to document subject consent) or the same mistake being made after a corrective plan has been issued to the investigator for previous findings of noncompliance. The convened IRB will make the final determination as to whether the noncompliance is continuing. For DoD supported research continuing noncompliance is inclusive of the following: a) a pattern of noncompliance that suggests the likelihood that, without intervention, instances of noncompliance will recur; b) a repeated unwillingness to comply with DoD Instruction 3216.02 or a persistent lack of knowledge of how to comply with this Instruction.

Noncompliance, Serious: Noncompliance that creates increased risks to subjects, adversely affects the rights and/or welfare of the subjects, or affects the scientific integrity of a study. Willful violations of IRB policies and /or Federal regulations including those pertaining to obtaining informed consent, reporting of unanticipated problems, and disclosure to subjects of risks associated with a study are also considered serious noncompliance. The convened IRB will make the final determination as to whether the noncompliance is serious. For DoD supported research serious noncompliance is inclusive of the following: a) failure of a person, group, or institution to act in accordance with DOD Instruction 3216.02 and its references such that the failure could adversely affect the rights, safety, or welfare of a human subject; place a human subject at increased risk of harm; cause harm to a human subject; affect a human subject's willingness to participate in research; or damage or compromise the scientific integrity of research.

Noninvasive: When applied to a diagnostic device or procedure, means one that does not by design or intention: 1) penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra or 2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of 21 CFR 812, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered noninvasive.

Parent: A child's biological or adoptive parent

Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research/clinical investigation.

Pharmacy and Therapeutics Committee: The committee charged with overseeing and managing medication formulary, medication errors, adverse drug events and medication protocols.

Pregnancy: The period of time from implantation until delivery. (See Vulnerable Population, Pregnant Woman)

Principal Investigator: An individual who the IRB determines is qualified to conduct a research project and who assumes primary responsibility for the ethical, scientific and administrative aspects of the proposed project and project staff.

Prisoner of War: A prisoner of war (POW, PoW, PW, P/W, WP, PsW, enemy prisoner of war (EPW) or "Missing-Captured) is a person, whether combatant or non-combatant, who is held in custody by an enemy power during or immediately after an armed conflict. This includes any person captured, detained, held, or otherwise under the control of Department of Defense (DoD) personnel (military and civilian, or contractor employee) except DoD personnel held for law enforcement purposes.

Privacy Certificate: Regulations at 28 CFR 22 require all applicants for National Institute of Justice (NIJ) support to submit a Privacy Certificate as a condition of approval of a grant application or contract proposal that contains a research or statistical component under which personally identifiable information will be collected. However, NIJ by policy requires the Certificate for all proposals regardless of whether the project involves the collection of identified data. In cases where no personally identifiable information will be collected, the Privacy Certificate should contain a statement to this effect. The Privacy Certificate is the applicant's assurance that he/she understands his/her responsibilities to protect the confidentiality of research and statistical information and has developed specific procedures to ensure that this information is only used or revealed in accordance with 42 USC 3789 and 28 CFR 22 which provide that research and statistical information identifiable to a private person is immune from legal process and may only be used or revealed for research purposes.

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 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.

Protected Health Information: Individually identifiable health information.

Protocol – Protocol is inclusive of all documents, processes and procedures associated with the study that have been presented to the IRB for approval (e.g. the IRB application, consent form, recruitment material, protocol, amendments etc.).

Quorum: A majority of IRB committee members present at a meeting (in person or via teleconference), including a non-scientific IRB member.

Registry: A registry is used in research for the collection and maintenance of information on individuals who have a similar condition and who will consent to being contacted regarding participation in future studies.

Repository: A repository is used in research for the collection and storage of identifiable specimens. By participating in the repository, the subjects consent to be contacted for possible participation in future studies that make use of identifiable samples.

Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Research, Engaged In: An institution becomes "engaged" in human subjects research when its employees or agents (i) intervene or interact with living individuals for research purposes or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)]. An institution is automatically considered to be "engaged" in human subjects research whenever it receives a direct DHHS award to support such research. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.

Research Involving a Human Being as an Experimental Subject: See Experimental Subject

Risk, Minimal: 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. The phrase "ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests " shall not be interpreted to include the inherent risks certain categories of human subjects face in their every day life. For example, the risks imposed in research involving human subjects focused on a special populations 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).

Risk, Minimal for Prisoners: 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.

Secretary: The Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

Serious Disease or Condition (21 CFR 312.300)**:** A disease or condition associated with morbidity that has substantial impact on da-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.

Service Members: Individuals appointed, enlisted, or inducted for military service under the authority of the Department of Defense. The Military Services are the Army, the Navy, the Air Force, the Marine Corps, the Coast Guard, and the Reserve Components, which includes the Army and the Air National Guards of the U.S. Members of the Reserve Components are included when in a duty status.

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 o f hearing, paralysis or stroke.

Significant Financial Interest: As defined in Institutional Policy 2006-01

Sponsor: A person or other entity that takes responsibility for and initiates a clinical investigation, or that funds extramural research. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator.

Sponsor (21 CFR 312.305(c)(2)): As related to expanded access, an individual or entity that submits an expanded access IND or protocol.

Sponsor-Investigator: 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.

Sponsor-Investigator (21 CFR 312.305(c)(3)): As related to expanded access, a licensed physician under whose immediate direction an investigational drug is administered or dispensed, and who submits an IND for expanded access use

Subinvestigator: See Co-investigator

Suspension: A temporary hold on any or all research activity associated with a study, or a permanent stop to some portion of a previously approve research activity placed by the IRB or other institutional official. For example, a hold placed on additional recruitment pending clarification of an adverse event would be considered a suspension of approval. Suspended protocols remain open and require continuing review.

Systematic Investigation: A formal scientific inquiry characterized by all of the following:

- the formulation of a hypothesis or experimental question
- the requirement of adherence to a predefined plan for the data collection and analysis
- the performance of data analysis to evaluate the hypothesis or experimental question
- the results of the inquiry are intended to be replicable

Terminal Condition: The final stage of an incurable or irreversible medical condition which, without the administration of a life support system, will result in death within a relatively short time, in the opinion of the attending physician (CT General Statute §19a-570(3)).

Termination: A permanent withdrawal of study approval by the IRB or institutional official that requires all study related activity to cease. It does not include a sponsor's decision to stop a study.

Test Article: Any drug for human use, 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 FDA or Public Health Service Act.

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

Treatment: The provision, coordination, or management of health care and related services by one or more health care providers, including the coordination or management of health care by a health care provider with a third party; consultation between health care providers relating to the patient; or the referral of a patient for health care form one heath care provider to another. (45 CFR 164)

Treatment Relationship, Direct: A treatment relationship between an individual and a health care provider that is not an indirect treatment relationship. (45 CFR 164)

Treatment Relationship, Indirect: A relationship between an individual and a health care provider in which: (1) the health care provider delivers health care to the individual based on the orders of another health care provider; and (2) the health care provider typically provides services or products, or reports the diagnosis or results associated with the health care, directly to another health care provider, who provides the services or products or reports to the individual. (45 CFR 164)

Unanticipated Problem Involving Risk to Subjects or Others (UP): Any unforeseen occurrence that involves risk to the subject or others (e.g. family member of subject, member of the research team, community at large etc.) that is related to or is possibly related to either a research intervention or interaction, or the conduct of the study in general. This definition is inclusive of unexpected, serious adverse events that are, or that may be, related to the research intervention. This definition is inclusive of expected, adverse events for which the overall profile of frequency and/or severity has been greater than expected. The convened IRB will make the final determination as to whether an instance represents a UP.

> Examples of unanticipated problems involving risk include, but are not limited to, an accidental or unintentional change to the IRB-approved protocol (e.g. administering the wrong dose of a drug, the delay or contamination of a drug shipment that will impact the timing of a treatment trial etc.), a complaint from a subject that indicates an unanticipated risk (e.g. loss of employment due to inadvertent disclosure of confidential data such as drug use etc.), unexpected changes to the risk/benefit profile of the study (e.g. based on literature, safety reports, interim results or other findings), unforeseen events involving the research team (e.g., the loss of a laptop computer with identifiable subject information, sudden unavailability of the PI and/or co-investigator etc.); unexpected internal serious adverse events that in the opinion of the PI may be related to the study intervention; unexpected external serious adverse events that the sponsor has deemed to be an unanticipated problem, or any change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research subject when the immediate hazard is, in the opinion of the PI, related to the study.

Undue Influence: Occurs when a person in a fiduciary capacity or in a position of authority misuses their trust or power in order to unfairly induce a party to enter into an agreement (e.g. sign an informed consent form) or to unfairly influence the decision making process (e.g. senior faculty member pressuring junior member to sway IRB vote for approval of a study).

Use: With respect to individually identifiable health information the sharing, employment, application, utilization, examination, or analysis of such information within an entity that maintains such information.

Vulnerable Population - Children: Persons who have not attained the legal age for consent to treatments or procedures involved in the research/clinical investigations, under the applicable law of the jurisdiction in which the research/clinical investigations will be conducted. When research is conducted in Connecticut, persons who meet this definition are all individuals under 18 years of age with the following exceptions:

1. Individuals between 16 and 18 years of age adjudicated as emancipated by a probate court
2. All individuals under 18 years of age, if the research procedures are limited to:
    - HIV testing, counseling, and treatment
    - Outpatient mental health services
    - Testing or treatment for sexually transmitted diseases
    - Treatment or rehabilitation for alcohol or drug dependence
    - Abortion counseling and treatment
3. All individuals between 16 and 18 years of age, if the research procedures are limited to:
    - Inpatient mental health services
4. All individuals between 17 and 18 years of age, if the research procedures are limited to donation of blood or any component thereof and to the withdrawal of blood in conjunction with any voluntary blood donation program.

When research is conducted outside of Connecticut, and review and approval by a local IRB or its equivalent is not required, the investigator must consult with legal counsel regarding the definition of child in the jurisdiction

Vulnerable Population - Decisionally Impaired: Having a severe psychiatric disorder (e.g. psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g. 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 the ability to make decisions in their best interest.

Vulnerable Population - Fetus: The product of conception from implantation until delivery.

Vulnerable Population - Fetus, dead: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

Vulnerable Population - Neonate: A newborn.

Vulnerable Population - Neonate, nonviable: A neonate after delivery that, although living, is not viable.

Vulnerable Population - Neonate, viable: Being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Vulnerable Population – Pregnant Woman: A woman shall be assumed pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery (Also see Pregnancy)

Vulnerable Population - Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Vulnerable Population - Terminally Ill: A person who is deteriorating from a life-threatening disease or condition for which no effective standard treatment exists. (also see Terminal Condition)

Vulnerable Population - Ward: A person (usually a minor) who has a guardian appointed by the court to care for and take responsibility for that person. A governmental agency may take temporary custody of a minor for his/her protection and care if the child is suffering from parental neglect or abuse, or has been in trouble with the law. Such a child is a "ward of the court" (if the custody is court-ordered) or a "ward of the state."

Procedure

This document is to be referenced for all official definitions of terms used within policies issued by the Human Subjects Protection Office.

Related Policies

Policies issued by the Human Subjects Protection Program

Basis

45 CFR 46 – Protection of Human Subjects
21 CFR 50 – Protection of Human Subjects
21 CFR 56 – Institutional Review Boards
45 CFR 164 – Privacy of Individually Identifiable Health Information
DOD Directive 3216.02
CT Statutes
Accreditation Standards

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Reviewed and Approved By:

Signed by Richard Simon 1/27/17
Richard Simon, MD **Date**
Director Human Subjects Protection Office