

GLOSSARY

1. **510(K) DEVICE** A medical device that is considered substantially equivalent to a device that was or is being legally marketed. A Sponsor planning to market such a device must submit notification to the FDA 90 days in advance of placing the device on the market. If the FDA concurs with the Sponsor, the device may then be marketed. 510(k) is the section of the Food, Drug and Cosmetic Act that describes pre-market notification; hence the designation "510(k) device."
2. **ABUSE-LIABLE** Pharmacological substances that have the potential for creating abusive dependency. Abuse-labile substances can include both illicit drugs (e.g., heroin) and licit drugs (e.g., methamphetamines).
3. **ADVERSE EVENT** Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.
4. **AGENTS OF THE ORGANIZATION** Agents are defined as individuals performing institutionally-designated activities or exercising institutionally-delegated authority or responsibility.
5. **AMENDMENT** A change, revision, modification to any item that was previously approved by the IRB (e.g. protocol, informed consent document, advertisement)
6. **ANONYMITY** The condition that exists when there are no identifiers on research materials that could link or identify the data to an individual subject even to the research investigators.
7. **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.
8. **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.
9. **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.
10. **AUTONOMY** Personal capacity to consider alternatives, make choices, and act without undue influence or interference of others.
11. **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.

12. **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.
13. **BENEFIT** A valued or desired outcome; an advantage.
14. **BIOLOGIC** Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries.
15. **BLIND STUDY DESIGNS** *See: Masked Study Designs; Double-Masked Design; and Single-Masked Design.*
16. **BOARD** *See: Institutional Review Board.*
17. **CASE-CONTROL STUDY** A study comparing persons with a given condition or disease (the cases) and persons without the condition or disease (the controls) with respect to antecedent factors. (*See also: Retrospective Studies.*)
18. **CDC** Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services.
19. **CHILDREN** Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted.
20. **CLASS I, II, III DEVICES** Classification by the Food and Drug Administration of medical devices according to potential risks or hazards.
21. **CLINICAL TRIAL** A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.
22. **CODE OF FEDERAL REGULATIONS (CFR)** The federal compendium of regulations on numerous topics related to compliance with federal laws.
23. **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.
24. **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.

25. **COMPENSATION** Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. (*Compare: Remuneration.*)
26. **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.*)
27. **CONFIDENTIALITY** Pertains to privacy and non-disclosure of personal 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.
28. **CONFLICT OF INTEREST** A conflict of interest is defined as: a close personal or professional association with the submitting Investigator(s), direct participation in the research (e.g., protocol development, Principal or Sub-Investigator), or any significant financial interest in the sponsoring company defined as \$10,000 or 5% ownership by the Investigators or their immediate family.
29. **CONSENT** *See: Informed Consent.*
30. **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. (*Compare: Grant.*)
31. **CONTRAINDICATED** Pertains to the use of a treatment that should not be used in certain individuals or conditions due to risks of disadvantageous, perhaps dangerous results (e.g., a drug may be contraindicated for pregnant women and persons with high blood pressure).
32. **CONTROL (SUBJECTS) OR CONTROLS** Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of study. Control conditions may be concurrent (occurring more or less simultaneously with the condition under study) or historical (preceding the condition under study). When the present condition of subjects is compared with their own condition on a prior regimen or treatment, the study is considered historically controlled.
33. **CORRESPONDENCE WITH EXTERNAL AGENCIES** Shall mean any letters, memos or emails sent to agencies of the federal government, funding agencies whether private or public or their agents.

34. **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.
35. **DATA AND SAFETY MONITORING BOARD (DSMB)** A 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.
36. **DEAD FETUS** An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached). Generally, some organs, tissues, and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.
37. **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.)
38. **DECISIONS MADE BY CHAIRPERSON** Shall mean any letters, memos or email sent representing the decision or opinions of the Chairperson of the IRB or their respective designee as long as such correspondence does not imply review and approval of research subjects.
39. **DECLARATION OF HELSINKI** A code of ethics for clinical research approved by the World Medical Association in 1964 and widely adopted by medical associations in various countries. It has been revised several times, most recently in October, 2000.
40. **DEPENDENT VARIABLES** The outcomes that are measured in an experiment. Dependent variables are expected to change as a result of an experimental manipulation of the independent variable(s).
41. **DESCRIPTIVE STUDY** Any study that is not truly experimental (e.g., quasi-experimental studies, correlation studies, record reviews, case histories, and observational studies).
42. **DESIGNATED STAFF** Shall mean staff designated by the Institutional Official in writing.
43. **DEVICE (MEDICAL)** *See: Medical Device.*
44. **DHHS** Abbreviation for U.S. Department of Health and Human Services.

45. **DIAGNOSTIC (PROCEDURE)** Tests used to identify a disorder or disease in a living person.
46. **DOUBLE-MASKED 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-blind."
47. **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.
48. **EMANCIPATED MINOR** A legal status conferred upon persons who have not yet attained the age of legal competency 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. (*See also: Mature Minor.*)
49. **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). (*See also: Fetus.*)
50. **EMERGENCY USE** 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 IRB approval.
51. **EPIDEMIOLOGY** A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population.
52. **EQUITABLE** Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed.
53. **ETHICS ADVISORY BOARD** An interdisciplinary group that advises the Secretary, HHS, on general policy matters and on research proposals (or classes of proposals) that pose ethical problems.
54. **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. (*See also: Fieldwork.*)
55. **EXCULPATORY** Pertaining to that which relieves of a responsibility, obligation, or hardship; clearing from accusation or blame.
56. **EXPANDED AVAILABILITY** Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.
57. **EXPEDITED REVIEW** Review of proposed research by IRB Chairperson 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.

58. **EXPERIMENTAL STUDY** A true experimental study is one in which subjects are randomly assigned to groups that experience carefully controlled interventions manipulated by the experimenter according to a strict logic allowing causal inference about the effects of the interventions under investigation. (*See also: Quasi-Experimental Study*).
59. **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. (*See also: Research.*)
60. **EXPERIMENTAL SUBJECT** See *Research Involving a Human Being as an Experimental Subject*
61. **FAMILY MEMBER** One who is part of the basic unit in society traditionally consisting of two parents rearing their own or adopted children; *also*: any of various social units differing from but regarded as equivalent to the traditional family
62. **FEDERAL POLICY (THE)** The federal policy that provides regulations for the involvement of human subjects in research. The policy applies to all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that takes appropriate administrative action to make the policy applicable to such research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the "Common Rule.")
63. **FETAL MATERIAL** The placenta, amniotic fluid, fetal membranes, and umbilical cord.
64. **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. The term "fetus" generally refers to later phases of development; the term "embryo" is usually used for earlier phases of development. (*See also: Embryo.*)
65. **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). (*See also: Ethnographic Research.*)
66. **FOOD AND DRUG ADMINISTRATION (FDA)** An agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.
67. **FULL IRB REVIEW** Review of proposed research at a convened meeting where the majority of the membership of the IRB is present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a

majority of those members present at the meeting.

68. **GENE THERAPY** The treatment of genetic disease accomplished by altering the genetic structure of either somatic (nonreproductive) or germ line (reproductive) cells.
69. **GENERAL CONTROLS** Certain FDA statutory provisions designed to control the safety of marketed drugs and devices. The general controls include provisions on adulteration, misbranding, banned devices, good manufacturing practices, notification and record keeping, and other sections of the Medical Device Amendments to the Food, Drug and Cosmetic Act.
70. **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.
71. **GENOTYPE** The genetic constitution of an individual.
72. **GRANT** Financial support provided for research study designed and proposed by the Principal Investigator(s). The granting agency exercises no direct control over the conduct of approved research supported by a grant. (*Compare: Contract.*)
73. **GUARDIAN** An individual who is authorized under applicable state or local law to give permission on behalf of a child or cognitively impaired individual to general medical care when general medical care includes participation in research. A guardian also means an individual who is authorized to consent on behalf of a child or cognitively impaired individual to participate in research.
74. **HELSINKI DECLARATION** *See: Declaration of Helsinki.*
75. **HHS** *See: DHHS.*
76. **HISTORICAL CONTROLS** Control subjects (followed at some time in the past or for whom data are available through records) who are used for comparison with subjects being treated concurrently. The study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.
77. **HUMAN PARTICIPANTS** Under the DHHS regulations, human subjects are defined as: living individual(s) about whom an Investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.
- Under the FDA regulations, human subjects are defined as: individuals who are or become participants in research, either as recipients of the test article or as controls. A subject may be either a healthy individual or a patient. For research involving medical devices, a human subject is also an individual on whose specimen an investigational device is used.
- Under the VA regulations, human subjects are living individuals

about whom an investigator conducting research obtains data through intervention or interaction with the individuals or through identifiable private information. As required by 38 CFR 16.102(f) an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

78. **IDE** *See: Investigational Device Exemptions.*
79. **IN VITRO** Literally, "in glass" or "test tube;" used to refer to processes that are carried out outside the living body, usually in the laboratory, as distinguished from in vivo.
80. **IN VIVO** Literally, "in the living body;" processes, such as the absorption of a drug by the human body, carried out in the living body rather than in a laboratory (in vitro).
81. **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. (*See also: Incompetence.*)
82. **INCOMPETENCE** Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (*See also: Incapacity.*)
83. **IND** *See: Investigational New Drug.*
84. **INFORMATION, PRIVATE** 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.
85. **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.
86. **INSTITUTION** (1): Any public or private entity or agency (including federal, state, and local agencies).

(2): 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.

87. **INSTITUTIONAL REVIEW BOARD** A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.
88. **INSTITUTIONALIZED COGNITIVELY IMPAIRED** Persons who are confined, either voluntarily or involuntarily, in a facility for the care of the mentally or otherwise disabled (e.g., a psychiatric hospital, home, or school for the retarded).
89. **INSTITUTIONALIZED** Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).
90. **INTERACTION** In the context of research, interaction includes communication (including conversations, monitoring, gathering, or recording of data, which occurs via telephone, e-mail, or other electronic device) or interpersonal contact between the investigator, and or member of the research staff, or other individual who is gathering and recording data for a research study.
91. **INTERVENTION** In research, intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
92. **INVESTIGATIONAL DEVICE EXEMPTIONS (IDE)** Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations.
93. **INVESTIGATIONAL NEW DRUG (IND) OR DEVICE (IDE)** 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.
94. **INVESTIGATOR** In clinical trials, an individual who actually conducts an investigation. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the Investigator. (See also: *Principal Investigator*.)
95. **IRB** See: *Institutional Review Board*.
96. **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.
97. **KEY PERSONNEL** Key personnel are individuals who provide study-related services or assistance and who have knowledge of the study protocol and the identity of study participants or their protected health information. Key personnel include principal investigators, co-principal investigators, sub-investigators, and research coordinators, and individuals from an affiliated institution.
98. **LEGALLY AUTHORIZED** A person authorized either by statute or by court appointment to

REPRESENTATIVE	make decisions on behalf of another person. In human subjects research, 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.
99. LONGITUDINAL STUDY	A study designed to follow subjects forward through time.
100 MASKED STUDY DESIGNS	Study designs comparing two or more interventions in which either the Investigators, the subjects, or some combination thereof do not know the treatment group assignments of individual subjects. Sometimes called "blind" study designs. (<i>See also: Double-Masked Design; Single-Masked Design.</i>)
101 MATURE MINOR	Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (<i>e.g.</i> , consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (<i>See also: Emancipated Minor.</i>)
102 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.
103 MENTALLY DISABLED	<i>See: Cognitively Impaired.</i>
104 MINIMAL RISK	<p>A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed 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 example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.</p> <p>The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults.</p>
105 MONITORING	The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.
106 NATIONAL COMMISSION	National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. An interdisciplinary advisory body, established by Congressional legislation in 1974, which was in existence until 1978, and which issued a series of reports and recommendations on ethical issues in research and medicine, many of which are now embodied in federal regulations.
107 NDA	<i>See: New Drug Application.</i>
108 NEONATE	Means a newborn

- 109 **NEW DRUG APPLICATION** Request for FDA approval to market a new drug.
- 110 **NIAAA** National Institute on Alcohol Abuse and Alcoholism; an institute in NIH.
- 111 **NIDA** National Institute on Drug Abuse; an institute in NIH.
- 112 **NIH** National Institutes of Health: a federal agency within the Public Health Service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research.
- 113 **NIJ** NIJ is the research, development and evaluation agency of the U.S. Department of Justice and is dedicated to researching crime control and justice issues.
- 114 **NIMH** National Institute of Mental Health; an institute in NIH.
- 115 **NONAFFILIATED 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).
- 116 **NONSIGNIFICANT RISK DEVICE** An investigational medical device that does not present significant risk to the patient. (*See also: Significant Risk Device.*)
- 117 **NONTHERAPEUTIC RESEARCH** Research that has no likelihood or intent of producing a diagnostic, preventive, or therapeutic benefit to the current subjects, although it may benefit subjects with a similar condition in the future.
- 118 **NONVIABLE NEONATE** An expelled or delivered neonate which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy. Although it may be presumed that an expelled or delivered neonate is nonviable at a gestational age less than 20 weeks and weight less than 500 grams, a specific determination as to viability must be made by a physician in each instance. (*See also: Viable Infant.*)
- 119 **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.
- 120 **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.

- 121 **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.
- 122 **OFFICE FOR HUMAN RESEARCH PROTECTIONS (OHRP)** The office within the Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects.
- 123 **OPEN DESIGN** An experimental design in which both the Investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.
- 124 **PATERNALISM** Making decisions for others against or apart from their wishes with the intent of doing them good.
- 125 **PERMISSION** The agreement of parent(s) or guardian to the participation of their child or ward in research.
- 126 **PHARMACOLOGY** The scientific discipline that studies the action of drugs on living systems (animals or human beings).
- 127 **PHASE 1 TRIALS** Includes 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.
- 128 **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 (Phases 2 and 3), to post-marketing studies (Phase 4).
- 129 **PHASE 2 TRIALS** Includes 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.

- 130 PHASE 3 TRIALS** Involves 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 an 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.
- 131 PHASE 4 TRIALS** Studies conducted after a drug has been approved by FDA, 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.
- 132 PHENOTYPE** The physical manifestation of a gene function.
- 133 PHS** Public Health Service. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.
- 134 PLACEBO** An inert substance or sham activity used in the guise of treatment; used in controlled clinical trials as a comparator to determine if an investigational therapy is more effective than no treatment.
- 135 PLANNED EMERGENCY RESEARCH** Planned research in a life-threatening emergency where the requirement to obtain prospective informed consent has been waived and is covered by 21 CFR 50.24. The research plan must be approved in advance by the FDA or DHHS and the IRB, and project, as well as its results, are publicly disclosed to the community in which the research is conducted.
- 136 PRECLINICAL INVESTIGATIONS** Laboratory and animal studies designed to test the mechanisms, safety, and efficacy of an intervention prior to its applications to humans.
- 137 PREGNANCY** The period of time from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (*i.e.*, has been delivered). Implantation is confirmed through a presumptive sign of pregnancy such as missed menses or a positive pregnancy test. This "confirmation" may be in error, but, for research purposes, investigators would presume that a living fetus was present until evidence to the contrary was clear. Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a

definition of pregnancy based on implantation necessary.

138 **PREMARKET APPROVAL**

Process of scientific and regulatory review by the FDA to ensure the safety and effectiveness of Class III devices.

139 **PRESIDENT'S COMMISSION**

President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. An interdisciplinary advisory group, established by congressional legislation in 1978, which was in existence until 1983, and which issued reports on ethical problems in health care and in research involving human subjects.

140 **PRINCIPAL INVESTIGATOR**

The scientist or scholar with primary responsibility for the design and conduct of a research project. (*See also: Investigator.*)

141 **PRISONER**

An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (*e.g.*, for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution.

The definition of minimal risk for research involving prisoners differs somewhat from that given for non-institutionalized adults.

142 **PRISONER OF WAR**

Department of the Navy regulations at SECNAVINST 3900.39D, define a Prisoner of War (POW) as a detained person as defined in Articles 4 and 5 of the Geneva Convention Relative to the Treatment of Prisoners of War of August 12, 1949. In particular, one who, while engaged in combat under orders of his government is captured by the armed forces of the enemy.

Department of the Army regulations at 70-25, define a Prisoner of War, under *Prisoner*, as any person (adult or minor) involuntarily confined or detained in a penal or correctional institution (for example, jail, workhouse, house of detention, prison, military stockade, or brig). The term is intended to encompass individuals detained pending arraignment, trial, or sentencing; and prisoners of war including detained personnel).

For other DoD Components, the definition of Prisoner of War will be specific to the DoD component regulation.

Under VA regulations, a **former prisoner of war** (POW) is defined in Title [38 U.S.C. 101\(32\)](#) as a person who, while serving in the active military, naval, or air service, was forcibly detained or interned in the line of duty by:

- an enemy government or its agents, or a hostile force, during a period of war, or
- a foreign government or its agents, or a hostile force, under circumstances which the Secretary finds to have been comparable to the circumstances under which persons have generally been

forcibly detained or interned by enemy governments during periods of war.

- 143 **PRIVACY** Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.
- 144 **PRIVATE INFORMATION** 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.
- 145 **PROBAND** The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.
- 146 **PROPHYLACTIC** Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.
- 147 **PROSPECTIVE STUDIES** Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.
- 148 **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.
- 149 **QUASI-EXPERIMENTAL STUDY** A study that is similar to a true experimental study except that it lacks random assignments of subjects to treatment groups. (*See also: Experimental Study.*)
150. **RADIOACTIVE DRUG** Any substance defined as a drug in the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Included are any non-radioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products." Drugs such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radio nuclides are not considered radioactive drugs.

151. **RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC)** An institutional committee responsible for the use of radioactive drugs in human subjects for research purposes. Research involving human subjects that proposes to use radioactive drugs must meet various FDA requirements, including limitations on the pharmacological dose and the radiation dose. Furthermore, the exposure to radiation must be justified by the quality of the study and the importance of the information it seeks to obtain. The committee is also responsible for continuing review of the drug use to ensure that the research continues to comply with FDA requirements, including reporting obligations. The committee must include experts in nuclear medicine and the use of radioactive drugs, as well as other medical and scientific members.
152. **RADIO-PHARMACEUTICAL** Drug (compound or material) that may be labeled or tagged with a radioisotope. These materials are largely physiological or sub-pharmacological in action, and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the consequent radiation exposure to the body or to specific organ systems when they are injected into the body.
153. **RANDOM RANDOM ASSIGNMENT RANDOMIZATION RANDOMIZED** 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.
154. **RECOMBINANT DNA TECHNOLOGY** DNA resulting from the insertion into the chain, by chemical or biological means, of a sequence (a whole or partial chain of DNA) not originally (biologically) present in that chain. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.
155. **RECUSE** To disqualify (oneself) as judge in a particular case; *broadly*: to remove (oneself) from participation to avoid a conflict of interest.
156. **REMUNERATION** Payment for participation in research. (NOTE: It is wise to confine use of the term "compensation" to payment or provision of care for research-related injuries.) (*Compare: Compensation.*)
157. **RESEARCH** Research as defined by DHHS regulations is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. A research project generally is described in a protocol that sets forth explicit objectives and formal procedures designed to reach those objectives.
- Research as defined by FDA regulations is any experiment that involves a test article and one or more human subjects, and is subject to requirements for prior submission to the FDA that either must meet

the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Food, Drugs, and Cosmetics Act, or need not meet the requirements for prior submission to the FDA under these sections of the Food, Drug, and Cosmetics Act, but the results of which are intended to be later submitted to, or held for inspections by, the FDA as part of an application for a research or marketing permit. For research involving drugs, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. The terms research, clinical research, clinical study, study and clinical investigation are synonymous.

Research as defined by VA regulations is the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question.

158. **RESEARCH INVOLVING A HUMAN BEING AS AN EXPERIMENTAL SUBJECT**
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 [32 CFR 219.102(f), reference (c)]. Examples include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, or the withholding of an intervention that would have been undertaken if not for the research purpose.
159. **RESPECT FOR PERSONS**
An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and those persons with diminished autonomy is protected.
160. **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.
161. **REVIEW AND APPROVAL OF RESEARCH PROJECTS**
Any action or decision taken by the IRB through full or expedited review mechanisms, which grants or may appear to grant Investigators with initial or continuing approval or research, training or educational projects involving human subjects.
162. **REVIEW (OF RESEARCH)**
The concurrent oversight of research on a periodic basis by an IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis.
163. **RISK**
The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." (*See also: Minimal Risk.*)
164. **ROUTINE INTERNAL CORRESPONDENCE**
Means any action, letters, memos or emails between the IRB and staff and members of the faculty or staff of the institution/organization that provides information concerning the review of research protocols by the IRB or staff which do not imply or appear to imply approval of

- this activity.
165. **SCIENTIFIC REVIEW GROUP** A group of highly regarded experts in a given field, convened by NIH to advise NIH on the scientific merit of applications for research grants and contracts. Scientific review groups are also required to review the ethical aspects of proposed involvement of human subjects. Various kinds of scientific review groups exist, and are known by different names in different institutes of the NIH (e.g., Study Sections, Initial Review Groups, Contract Review Committees, or Technical Evaluation Committees).
- 166 **SERIOUS ADVERSE EVENT** For FDA safety reporting purposes, any adverse drug experience occurring at any dose that results in any of the following outcomes: (1) Death, (2) a life-threatening adverse drug experience, (3) inpatient hospitalization or prolongation of existing hospitalization, (4) a persistent or significant disability/incapacity, or (5) a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.
- 167 **SIGNATURE STAMP** Shall mean a mechanical stamping device bearing the reproduction of the authorized individual's signature.
- 168 **SIGNIFICANT RISK DEVICE** An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.
- 169 **SINGLE-MASKED 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-blind design."
- 170 **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.
- 171 **SOCIAL EXPERIMENTATION** Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy.
- 172 **SPONSOR (OF A DRUG TRIAL)** A person or entity that initiates a clinical investigation of a drug — usually the drug manufacturer or research institution that developed the drug. The Sponsor does not actually conduct the investigation, but rather distributes the new drug to Investigators and physicians for clinical trials. The drug is administered to subjects under the immediate direction of an investigator who is not also a Sponsor. An Investigator may, however, serve as a Sponsor-Investigator. The

Sponsor assumes responsibility for investigating the new drug, including responsibility for compliance with applicable laws and regulations. The Sponsor, for example, is responsible for obtaining FDA approval to conduct a trial and for reporting the results of the trial to the FDA.

**173 SPONSOR-
INVESTIGATOR**

An individual who both initiates and actually conducts, alone or with others, a clinical investigation. Corporations, agencies, or other institutions do not qualify as Sponsor-Investigators.

**174 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. If the probability is less than or equal to a predetermined value (e.g., 0.05 or 0.01), then the null hypothesis is rejected at that significance level (0.05 or 0.01).

175 STUDY SECTION

See: Scientific Review Group.

176 SUBJECTS (HUMAN)

See: Human Participants.

177 SURVEYS

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

178 TEST ARTICLE

Any drug (including a biological product for human use), medical device for human use, or any other article subject to regulation by the Food and Drug Administration.

179 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 affected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.

180 THERAPY

Treatment intended and expected to alleviate a disease or disorder.

**181 UNANTICIPATED
PROBLEM INVOLVING
RISKS TO PARTICI-
PANTS OR OTHERS**

Any problem that (1) was unforeseen at the time of its occurrence and (2) indicates that participants are at increased risk of harm.

**182 UNIFORM
ANATOMICAL GIFT
ACT**

Legislation adopted by all 50 States and the District of Columbia that indicates procedures for donation of all or part of a decedent's body for such activities as medical education, scientific research, and organ transplantation.

183 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.

184 VARIABLE (NOUN)

An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention.

185 VIABLE INFANT

When referring to a delivered or expelled fetus, the term "viable infant" means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability. These indices depend on the state of present technology and may be revised periodically. (See also: *Nonviable Fetus*.)

186 VOLUNTARY

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

187 VULNERABLE SUBJECTS

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent.

APPROVED BY: _____ **DATE:** 01/15/2010

NEXT ESTABLISHED REVIEW DATE: MAY 2012