MUSC
Medical University of South Carolina

I. POLICY

A. Introduction

In order to ensure that terminology and definitions are consistent throughout the Human Research Protection Program, this document will serve as the source for terms and definitions. Subsequent references to terms and definitions will refer to this document.

B. Application

The definitions in this policy apply to all other policies established for the Protection of Human Subjects in Research.

C. DEFINITIONS

1. **ABUSE-LIABLE** – Pharmacological substances that have the potential for creating abusive dependency. Abuse able substances can include both illicit drugs (e.g., heroine) and licit drugs (e.g. methamphetamines).

2. **AD HOC** – For or concerned with one specific purpose or case; often improvised or impromptu.

3. **ADJUVANT THERAPY** – Therapy provided to enhance the effect of a primary therapy; auxiliary therapy.

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

5. **ADVERSE EVENT** – Expected or unexpected harmful events as a result of the use of an investigational or approved drug, biologic or device, or of an investigational procedure, observed in the approved project or in other research studies similar to that of the approved project.

6. **AGENT** – Person authorized to act on behalf of MUSC. This includes an individual performing MUSC designated activities or exercising MUSC-delegated authority or responsibility.

7. **ALLEGATION OF NON-COMPLIANCE** – An assertion of non-compliance that has yet to be proved or supported by evidence.

8. **ANONYMIZED SAMPLES (UNLINKED)** – Samples that may have been acquired from identified human sources, but for which all identifiers or codes have been removed and destroyed such that the ability to identify particular individuals, via clinical or demographic information, would be extremely difficult for the investigator, the repository or a third party.

9. **APPROVAL PERIOD** – Research involving human subjects may be approved for a maximum period of one year from the date of approval or for a shorter period of time, as determined by the IRB.

10. **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.

11. **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.

12. **AUTHORIZATION** – Express written permission that an individual permits the release and use of their individually identifiable health information for a particular purpose. Authorizations are not required to use an individual's health information to treat them, obtain payment or for a provider's health care operations. However, under HIPAA, research is not considered health care operations, and therefore, requires an authorization or waiver of authorization with limited exception. The provider (or investigator) is responsible for obtaining an authorization from an individual.

13. **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.

14. **AUTONOMY** – Personal capacity to consider alternatives, make choice, and act without undue influence or interference of others.

15. **AUTOPSY** Examination by dissection of the body of an individual to determine cause of death.

16. **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.

17. **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.

18. **BENEFIT** - A valued or desired outcome; an advantage.

19. **BIOLOGIC -** Any therapeutic serum, toxin, anti-toxin, or analogous microbial product applicable to the prevention, treatment, or cure of diseases or injuries.

20. **BLIND STUDY DESIGNS** - See: Masked Study Designs; Double-Masked Design; and Single-Masked Design.

21. **BOTANICAL DRUG PRODUCTS** consist of vegetable materials, which may include plant materials, algae, macroscopic fungi, or combinations thereof, that are intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in humans.

22. **CADAVER** - The body of a deceased person.

23. **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.).

24. **CAT SCAN** - Computerized Axial Tomography, an X-ray technique for producing images of internal bodily structures through the assistance of a computer.

25. **CDC** - Centers for Disease Control and Prevention; an agency within the Public Health Service, Department of Health and Human Services.

26. **CHILDREN** - Persons who have not attained the legal age for consent to treatment or procedures involved in the research or clinical investigations, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402(a) and 21 CFR 50.3(c)]. “Children” as defined by the state of South Carolina are individuals less than 18 years of age.

27. **CLASS I, II, III DEVICES** - Classification by the Food and Drug Administration to 510(k) medical devices based on the level of risk and, therefore, the level of FDA oversight needed to ensure the device is safe and effective as labeled (FDA Information Sheets, Medical Devices, 1998 Update).

28. **CLINICAL INVESTIGATION** – See definition for Research (as defined by FDA regulations).

29. **CLINICAL TRIAL** - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions or biomedical or behavioral health-related outcomes.

30. **CODE OF FEDERAL REGULATIONS (CFR)** – A codification of federal agency regulations which has the force and effect of law.

31. **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 (Institutional Review Board Guidebook, 1993). 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.

32. **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.

33. **COMMON RULE** – See: Federal Policy (The)

34. **COMPENSATION** - Payment or medical care provided to subjects injured in research; does not refer to payment (remuneration) for participation in research. (Compare: Remuneration.)

35. **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 (Institutional Review Board Guidebook, 1993). (See also: Incompetence, Incapacity).

36. **COMMUNITY BASED PARTICIPATORY RESEARCH (CBPR)** - a type of community-engaged research that is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. This type of research begins with a research topic of importance to the community and has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities. (W.K. Kellogg Foundation)

37. **COMMUNITY ENGAGED RESEARCH** - Community-engaged research is a framework or approach for conducting research, not a methodology in and of itself. It is characterized by the principles that guide the research and the relationships between the communities and academic researcher's community engaged research requires partnership development, cooperation and negotiation, and commitment to addressing local health issues.

38. **CONFIDENTIALITY -** Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure (IRB Guidebook, 1993). Further information: Joan E. Sieber "Privacy and Confidentiality: As Related to Human Research in Social and Behavioral Science (Research Involving Human Participants V2)" Online Ethics Center for Engineering 5/25/2007 12:04:01 PM National Academy of Engineering.

39. **CONFLICT OF INTEREST IN SCIENCE** refers to situations in which financial or other personal considerations (i.e. service on Board of Directors, Consulting, intellectual property related to protocol under consideration, protocol submitted by members of immediate family) may compromise, or have the appearance of compromising, an investigator's professional judgment in designing, conducting or reporting research (MUSC Conflict of Interest, Financial Disclosure).

40. **CONSENT** - See: Informed Consent.

41. **CONTINUING NONCOMPLIANCE** – a pattern of recurring or on-going instances of actions or omissions which indicates an underlying deficiency in knowledge of the regulations and/or IRB requirements and/or willingness to comply with them. In VA Research, continuing non-compliance is a persistent failure to adhere to the laws, regulations, or polcies governing human research. In all cases, the determination that non-compliance is continuing rests with the IRB.

42. **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.)

43. **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.

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

45. **CORRECTIVE ACTIONS** – Suggestions for corrections or improvements to be made to assure regulatory agency inspection readiness and alignment with regulations and standards and a listing of current good practices.

46. **CORRELATION COEFFICIENT** - A statistical index of the degree of relationship between two variables. Values of correlation coefficients range from -1.00 through zero to +1.00. A correlation coefficient of 0.00 indicates no relationship between the variables. Correlations approaching -1.00 or +1.00 indicate strong relationships between the variables. However, causal inferences about the relationship between two variables can never be made on the basis of correlation coefficients, no matter how strong a relationship is indicated.

47. **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.

48. **CUSTOM DEVICE –** A device that: [21CFR § 812.3(b)]
    a) Necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician;

b) Is not generally available to, or generally used by, other physicians;
c) Is not generally available in finished form for purchase or for dispensing upon prescription;
d) Is not offered for commercial distribution through labeling or advertising; and
e) Is intended for use by an individual patient named in the order of a physician, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician in the course of professional practice.

49. **DATA AND SAFETY MONITORING BOARD** - 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.

50. **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) [45 CFR 46.203(f)]. 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.

51. **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.)

52. **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 was revised in 1975 and 1989.

53. **DE-IDENTIFIED** – Health information is de-identified if there is no reasonable basis to believe that the data can be used to identify an individual, or if the provider has no reasonable basis to believe it can be used to identify the individual. The Privacy rule requires one of the two following approaches to de-identify data:
a) If a person with appropriate knowledge and experience applying generally accepted statistical and scientific principles and methods for rendering information not

individually identifiable makes a determination that the risk is very small that the information could be used, either by itself or in combination with other available information, by anticipated recipients to identify a subject of the information.

b) If all 18 identifiers have been removed, including name, all geographic subdivisions smaller than a State including street address, city, county, precinct, zip codes and equivalent geocodes, (except for the initial 3 digits of a zip code if more than 20,000 people reside in the area), all dates including birthdays (other than the year) and ages over 89, phone numbers, fax numbers, email addresses, social security numbers, medical record numbers, health plan beneficiary numbers, account numbers, certificate/license numbers, vehicle identifiers and serial numbers (including license plate number), device identifiers and serial numbers, URLs, IP addresses, biometric identifiers, full face photographic images and any comparable images, any other unique identifiers, characteristic or code.

NOTE: Other demographic information, such as gender, race, ethnicity, and marital status are not included in the list of identifiers that must be removed.

54. **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).

55. **DESCRIPTIVE STUDY** - Any study that is not truly experimental (e.g., quasi-experimental studies, correlation studies, record reviews, case histories, and observational studies).

56. **DEVICE (MEDICAL)** - See: Medical Device.

57. **DHEW** A federal agency: U.S. Department of Health, Education and Welfare; reorganized in 1980 as the Department of Health and Human Services (DHHS) and the Department of Education.

58. **DHHS** – U.S. Department of Health and Human Services

59. **DIAGNOSTIC (PROCEDURE)** - Tests used to identify a disorder or disease in a living person.

60. **DISSENT** – An individual's negative expressions, verbal and/or non-verbal that they object to participation in the research or research activities.

61. **DOUBLE-BLIND OR DOUBLE-MASKED DESIGN** - A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects.

62. **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.

63. **ELECTRONIC MEDIA** – The mode of electronic transmission, includes the Internet (wide-open), Extranet (using Internet technology to link a business with information only accessible to collaborating parties), leased lines, dial-up lines, private networks, and transmissions that are physically moved from one location to another using magnetic tape, disk, or compact disk media.

64. **EMANCIPATED MINOR** - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law (for such purposes as consenting to medical care), but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as being self-supporting and not living at home, marriage, or procreation. (See also: Mature Minor.)

65. **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.)

66. **EMERGENCY USE**
    a) The use of an investigation device in a patient : 1) there is an "exemption" from prospective IRB prior review and approval of the IND one time treatment use because there is insufficient time for the IRB to convene and review the request, and 2) the patient is in a life-threatening or severely debilitating position (21 CFR 56.102(d)). Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted. 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 IRB meeting is feasible (FDA Information Sheet, 1998).
    b) The use of an investigational device in a patient:
        (1) Who is in a life-threatening situation and,
        (2) Necessarily deviates from devices generally available or from an applicable performance standard or pre-market approval requirement in order to comply with the order of an individual physician;

(3) Is not generally available to, or generally used by, other physicians;
(4) Is not generally available in finished form for purchase or for dispensing upon prescription;
(5) Is not offered for commercial distribution through labeling or advertising; and
(6) Is intended for use by an individual patient named in the order of a physician, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician in the course of professional practice.

67. **ENCRYPTION** – The process of converting information, particularly information such as social security number and name that identifies individuals, into a code.

68. **ENGAGED IN RESEARCH** – being involved in one or more of the following activities: 1) Receiving an HHS award for research, 2) Intervening with participants for research purposes (invasive or noninvasive), 3) Manipulating the environment, 4) Interacting with participants for research purposes, and/or 5) Obtaining identifiable private information or identifiable biological specimens for any source for research purposes (OHRP Engagement of Institutions in Research at : http://www.hhs.gov/ohrp/policy/engage08.html

69. **EPIDEMIOLOGY** - A scientific discipline that studies the factors determining the causes, frequency, and distribution of diseases in a community or given population.

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

71. **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.

72. **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.)

73. **EXCULPATORY LANGUAGE -** language through which the subject waives or appears to waive the subject's legal rights or

releases or appears to release the investigator, sponsor, the institution, or its agents from liability for negligence (45 CFR 46.116).
(See http://www.hhs.gov/ohrp/policy/exculp.html for examples of exculpatory and acceptable language)

74. **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.

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

76. **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.)

77. **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).

78. **EXPERIMENTAL SUBJECT** – For research sponsored or funded by the U.S. Department of Defense (DoD), this is a living individual about whom an investigator is conducting research and obtaining data through intervention or interaction with the individual or identifiable private information. Limitations on the use of humans as experimental subjects are outlined in DOD Directive 3216.02.

79. **FALSE NEGATIVE** - When a test wrongly shows an effect or condition to be absent (e.g., that a woman is not pregnant when, in fact, she is).

80. **FALSE POSITIVE** - When a test wrongly shows an effect or condition to be present (e.g. that is woman is pregnant when, in fact, she is not).

81. **FDA** – U.S. Food and Drug Administration. An agency of the federal government established by Congress in 1912 and presently part of the Department of Health and Human Services.

82. **FEDERAL GUIDANCE** – Information published by federal agencies on the topic that represents the agency's current thinking or view but does not have the effect or force of law.

83. **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.")

84. **FEDERALWIDE ASSURANCE (FWA)** – A document filed with the Office for Human Research Protections (OHRP) of the Department of Health and Human Services expressing an institution's commitment to comply with the department's regulations for the protection of human subjects.

85. **FETAL MATERIAL -** The placenta, amniotic fluid, fetal membranes, and umbilical cord.

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

87. **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.)

88. **FINANCIAL INTEREST RELATED TO THE RESEARCH** – A financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

89. **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 premarket notification; hence the designation "510(k) device." (FDA Information Sheets, Medical Devices, 1998 Update).

90. **510(k) SUBMISSION** – The purpose of a 510(k) submission is to demonstrate that a device is “substantially equivalent” to a predicate device (one that has been cleared by the FDA or marketed before 1976). The 510(k) submitter compares and contrasts the subject and predicate devices, explaining why any differences between them should be acceptable.

91. **FTE** – Full-time equivalent appointment.

92. **FULL BOARD REVIEW** - Review of proposed research at a convened meeting at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. For the research to be approved, it must receive the approval of a majority of those members present at the meeting.

93. **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 [21 U.S. Code §360(c) (Food, Drug and Cosmetic Act §513)].

94. **GENERALIZABLE KNOWLEDGE –** Conclusions derived from a systematic investigation of a group of subjects (sample) that can be applied to populations beyond the one from which the sample is derived.

95. **GENE THERAPY** - The treatment of genetic disease accomplished by altering the genetic structure of either somatic (nonreproductive) or germline (reproductive) cells.

96. **GENETIC RESEARCH** – Research (not diagnostic testing) which involves either the analysis of human chromosomes or DNA from an individual an/or family members for the purpose of deriving information concerning the individual or family about the presence, absence or mutation of genes, DNA markers or inherited characteristics or other studies with the intent of collecting and evaluating information about heritable diseases and/or characteristics within a family.

97. **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.

98. **GENOTYPE** - The genetic constitution of an individual.

99. **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.)

100. **GREATER THAN MINIMAL RISK** – The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

101. **GUARDIAN** - An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care [45 CFR 46.402(e) and 21 CFR 50.3(s)].

102. **HELSINKI DECLARATION** - See: Declaration of Helsinki.

103. **HIPAA** – The Health Insurance Portability and Accountability Act of 1996. Also referred to as the Privacy Rule.

104. **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.

105. **HUMAN IN VITRO FERTILIZATION** - Any fertilization involving human sperm and ova that occurs outside the human body.

106. **HUMAN SUBJECT –**

a) **(as defined by DHHS and VA regulations)** – A living individual about whom an investigator (whether professional or student) is conducting research: (1) Obtains information or biospecimens through *intervention* or *interaction* with the individual and uses, studies, or analyzes the information or biospecimens or (2) Obtains, uses, studies, analyzes, or generates identifiable *private information or identifiable biospecimens*. *Intervention* includes both physical procedures by which data information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. *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. (The Common Rule [38 CFR 16.102(f)] which is identical to [45 CFR 46.102(f)(1)(2)]

b) **(as defined by FDA regulations)** – An individual who becomes a participant in research regulated by the Food and Drug Administration (FDA), either as a recipient of a test article or as a control. A subject may be either a healthy human or a patient. In the case of research involving medical devices, a human subject includes an individual on whose specimen a medical device is used. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

107. **HUMAN SUBJECTS RESEARCH** – Any activity that is either (a) "research" as defined by DHHS regulations that involves "human subjects" as defined by DHHS regulations or (b) "research" as defined by FDA regulations that involves "human subjects" as defined by FDA regulations.

108. **IDE** – See Investigation Device Exemption.

109. **IMMEDIATE FAMILY** – Refers to a person's spouse and dependent children.

110. **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.)

111. **INCOMPETENCE** - Technically, a legal term meaning inability to manage one's own affairs. Often used as a synonym for incapacity. (See also: Incapacity.)

112. **IND** – See Investigational New Drug.

113. **IDENTIFIABLE INFORMATION** – information where the identity of the subject is or may be readily be ascertained by the investigator or associated with the information.

114. **IDENTIFIED SAMPLES** – Biological samples obtained by an investigator or a 3rd party which have identifiers attached or a link

permitting determination of the individual subject source through the use of a code.

115. **IDENTIFIERS** – Information that can be used to link a sample or scientific result with a specific person or group of people. Examples include name, social security number, hospital number or other unique identifier. It should also be noted that using current information technology, a combination of descriptive data may be sufficient to allow identification of the donor and thereby collectively may be considered identifiers (e.g. zip code, birth date or profession may be sufficient to identify a specific individual.)

116. **INDEPENDENT VARIABLES** - The conditions of an experiment that are systematically manipulated by the investigator.

117. **INFORMED CONSENT** -
    a) A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence [Federal Regulations [45 CFR 46.116(a) and 21 CFR 50.20 and 50.25]].
    b) An active participatory process which involves three key features: a) disclosing to potential subjects information needed to make an informed decision, b) facilitating the understanding of what has been disclosed, and 3) promoting the "voluntariness" of the decision about whether or not to participate in the research (OHRP Informed Consent Frequently Asked Questions, http://answers.hhs.gov/ohrp/categories/1566
    c) The investigator must seek consent only under conditions that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence [45 CFR 46.116].

118. **INSTITUTION** –
    a) Any public or private entity or agency (including federal, state, and local agencies).
    b) 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.

119. **INSTITUTIONAL AUTHORIZATION AGREEMENT (IAA)** An IAA sets forth the terms and conditions under which one institution/facility may rely on the other for IRB review. Together with the FWA, this agreement allows many off campus community sites to rely on MUSC to act as the IRB of record in situations where the community site is engaged in research but does not have its own IRB.

120. **INSTITUTIONAL OFFICIAL (IO)** – The individual with the legal authority to represent the institution.

121. **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.

122. **INSTITUTIONALIZED** - Confined, either voluntarily or involuntarily (e.g., a hospital, prison, or nursing home).

123. **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).

124. **INTERACTION** includes communication or interpersonal contact between investigator and subject.

125. **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.

126. **INTERVENTIONAL CLINICAL RESEARCH** means any prospective biomedical or behavioral research study involving human subjects that is designed to answer specific questions about the safety, efficacy, and effectiveness of biomedical or behavioral interventions (NIH, PHS 398, Human Subjects Research Supplement, 2006).

127. **INVESTIGATIONAL DEVICE EXEMPTION** - (IDE) - An investigational device exemption (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 to FDA. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE **before** the study is initiated. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

128. **INVESTIGATIONAL DRUG OR DEVICE** –
    a) 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.
    b) A new drug or biologic drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms **investigational drug** and **investigational new drug** are deemed to be synonymous. [21 CFR 312.3(b)]
    c) An **investigational device** is a medical device that is the object of an investigation [21CFR § 812.3(g)], i.e., the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

129. **INVESTIGATIONAL PROCEDURES** – Any procedure tested for safety and effectiveness, not yet considered standard procedure for the particular use being researched.

130. **INVESTIGATOR** - In clinical trials, an individual who actually conducts an investigation [21 CFR 312.3]. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the investigator. (See also: Principal Investigator.)

131. **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.

132. **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).

133. **IRB** - See: Institutional Review Board.

134. **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.

135. **KEY PERSONNEL** – All individuals responsible for the design or conduct of the study. Everyone who has contact with human subjects, with confidential data about human subjects, or data that was obtained from human subjects, for research purposes is included.

136. **LACTATION** - The period of time during which a woman is providing her breast milk to an infant or child.

137. **LEGALLY AUTHORIZED REPRESENTATIVE** or **LEGAL REPRESENTATIVE** –
    a) A person authorized either by statute or by court appointment to 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 [21 CFR 50.3(l)].
    b) 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 procedures involved in the research [45 CFR 46.102(c)]. If there is no applicable law addressing this issue, the legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research. The legal representative must have documentation of this legal status.

138. **LEGAL GUARDIAN** - an individual who is authorized under applicable South Carolina law to consent on behalf of the child to general medical care [45 CFR 46.402 (e)]. A legal guardian may consent for a "ward" to participate in research in lieu of a child's adoptive or biological parents.

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

140. **LOD SCORE** - An expression of the probability that a gene and a marker are linked.

141. **LONGITUDINAL STUDY** - A study designed to follow subjects forward through time.

142. **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. (See also: Double-Blink or Double-Masked Design; Single-Blind or Single-Masked Design.)

143. **MATURE MINOR** - Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor. (See also: Emancipated Minor.)

144. **MEDICAL DEVICE** – An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
    a) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
    b) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
    c) intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

145. **MEDICAL DEVICE AMENDMENTS (MDA)** - Amendments to the Federal Food, Drug and Cosmetic Act passed in 1976 to regulate the distribution of medical devices and diagnostic products.

146. **MEDICAL DEVICE CLASS** - See **CLASS I, II, III DEVICES**

147. **MENTALLY DISABLED** - See: Cognitively Impaired.

148. **METABOLISM (OF A DRUG)** - The manner in which a drug is acted upon (taken up, converted to other substances, and excreted) by various organs of the body.

149. **MINIMAL RISK** - 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. [45 CFR 46.102(i)][21 CFR 56102(i)] The definition of minimal risk for research involving prisoners means 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. [See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners."]

150. **MINOR MODIFICATIONS** – Modifications to a research protocol which have minimal risk to study participants such as wording changes and correction of typographical errors. In order for minor modifications to be reviewed using the expedited process, modifications involving new procedures must involve no more than minimal risk and fall into one of the expedited categories (1)-(7) detailed in HRPP Program Guide Section 2.5 Expedited Review of Research Policy and Procedures.

151. **MINORS** – see Children.

152. **MONITORING** - The collection and analysis of data as the project progresses to assure the appropriateness of the research, its design and subject protections.

153. **MUSC –** Medical University of South Carolina

154. **MUSC Facilities** – Facilities owned and operated by MUSC.

155. **MUSC Institutional Official** – Individual authorized to act for MUSC and, on its behalf, obligates MUSC to the Terms of the Federalwide Assurance with the Department of Health and Human Services and OHRP.

156. **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.

157. **NDA** - See: New Drug Application.

158. **NEONATE** – A newborn baby less than 30 days old.

159. **NEW DRUG APPLICATION** - Request for FDA approval to market a new drug.

160. **NIAAA** - National Institute on Alcohol Abuse and Alcoholism; an institute in NIH.

161. **NIDA** - National Institute on Drug Abuse; an institute in NIH.

162. **NIH** – See National Institutes of Health.

163. **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.

164. **NIMH** - National Institute of Mental Health; an institute in NIH.

165. **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).

166. **NONCOMPLIANCE** with federal and/or state regulations or IRB requirements for human subject protections is evidenced by intentional or unintentional behavior demonstrating lack of adherence to these regulations/requirements.

167. **NON-SCIENTIFIC MEMBER** – Member whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline.

168. **NONSIGNIFICANT RISK DEVICE** - An investigational medical device that does not present significant risk to the patient and does not meet the definition of a significant risk study (FDA Information Sheets, Medical Devices, Updated 1998)... (See also: Significant Risk Device.)

169. **NON-SIGNIFICANT RISK (NSR) DEVICE STUDY** - A study of a device that does not meet the definition for a significant risk study.

170. **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.

171. **NONVIABLE FETUS** - An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy [45 CFR 46.203 (d) and (e)]. Although it may be presumed that an expelled or delivered fetus is nonviable at a

gestational age less than 20 weeks and weight less than 500 grams [Federal Register 40 (August 8, 1975): 33552], a specific determination as to viability must be made by a physician in each instance. (See also: Viable Infant.)

172. **NONVIABLE NEONATE –** A neonate after delivery that, although living is not viable [45 CFR 46.202].

173. **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.

174. **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.

175. **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.

176. **OFFICE FOR PROTECTION FROM RESEARCH RISKS (OPRR)** - The office within the National Institutes of Health, an agency of the Public Health Service, Department of Health and Human Services, responsible for implementing DHHS regulations (45 CFR Part 46) governing research involving human subjects. Reorganized to OHRP.

177. **OHRP** – *Office for Human Research Protections* of the Department of Health and Human Services.

178. **OPEN DESIGN** - An experimental design in which both the investigator(s) and the subjects know the treatment group(s) to which subjects are assigned.

179. **OPRR** - See: Office for Protection from Research Risks.

180. **PARENT** – A child's biological or adoptive parent.

181. **PARTICIPANT** – A living individual about whom a research investigator (whether a professional or a student) obtains data through intervention or interaction with the individual or from individually identifiable information. An individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A participant may be either a healthy human or a patient.

182. **PARTICIPATE** – Take part in the described activity in any capacity, including but not limited to serving as the Principal Investigator, co-investigator, research collaborator or provider of direct patient care. The term is not intended to apply to individuals who provide primarily technical support or who are purely advisory, with no direct access to the data (e.g., control over its collection or analysis) or, in the case of clinical research, to the trial participants, unless they are in a position to influence the study's results or have privileged information as to the outcome.

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

184. **PERMISSION** - The agreement of parent(s) or guardian to the participation of their child or ward in research [45 CFR 46.402(c)].

185. **PHARMACOLOGY** - The scientific discipline that studies the action of drugs on living systems (animals or human beings).

186. **PHASE 1, 2, 3, 4 DRUG TRIALS**- Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3), to postmarketing studies (Phase 4).
    a) ***PHASE 1 DRUG TRIAL -*** Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms

of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.

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

c) ***PHASE 3 DRUG TRIAL*** - Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide 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.

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

187. **PHENOTYPE** - The physical manifestation of a gene function.

188. **PHS PUBLIC HEALTH SERVICE**. Part of the U.S. Department of Health and Human Services, it includes FDA, NIH, CDC, SAMHSA, and HRSA.

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

190. **POSTAMENDMENTS DEVICES** - Medical devices marketed after enactment of the 1976 Medical Device Amendments.

191. **PREAMENDMENTS DEVICES** - Medical devices marketed before enactment of the 1976 Medical Device Amendments.

192. **PRECLINICAL INVESTIGATIONS** - Laboratory and animal studies designed to test the mechanisms, safety, and efficacy of an intervention prior to its applications to humans.

193. **PREDICATE DEVICES** - Currently legally marketed devices to which new devices may be found substantially equivalent under the 510(k) process.

194. **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 [45 CFR 46.203(b)]. 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.

195. **PREMARKET APPROVAL** - Process of scientific and regulatory review by the FDA to ensure the safety and effectiveness of Class III devices.

196. **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.

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

198. **PRISONER** –

a) An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statue; (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 [45 CFR 46.303(c)].

b) "Prisoner" is defined by HHS regulations at 45 CFR 46.303(c) as "any individual involuntarily confined or detained in a penal institution. Guidance provided by OHRP extends the definition to 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.

199. **PRIVACY** – Control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others (IRB Guidebook, 1993).

200. **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. [45 CFR 46.102(f)(1)(2)]

201. **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.

202. **PROPHYLACTIC** - Preventive or protective; a drug, vaccine, regimen, or device designed to prevent, or provide protection against, a given disease or disorder.

203. **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.

204. **PROTECTED HEALTH INFORMATION (PHI)** – Individually identifiable health information transmitted by electronic media, maintained in any electronic media, or transmitted or maintained in any other form or medium.

205. **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.

206. **PROTOCOL AMENDMENT** – Any change, clarification, advertisement, (including minor consent form changes) made to the approved protocol.

207. **PROTOCOL DEVIATION** – Any variance from the protocol involving a subject or subjects that is not approved by the IRB prior to its initiation or implementation, and occurs when a member of the study team departs from the IRB-approved protocol in any way **without the investigator first obtaining IRB approval**.

208. **PURITY** - The relative absence of extraneous matter in a drug or vaccine that may or may not be harmful to the recipient or deleterious to the product.

209. **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.)

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

211. **RADIOLOGY DEVICE** - A radiology device that is used as a diagnostic device, or is used as a therapeutic device, or has two or more types of uses (e.g., used both as a diagnostic device *and* a therapeutic device. See [21CFR § 892.1000 - 892.6500] for specific listings of device types for each category.

212. **RADIOPAQUE CONTRAST AGENTS** - Materials that stop or attenuate radiation that is passed through the body, creating an outline on film of the organ(s) being examined. Contrast agents, sometimes called "dyes," do not contain radioisotopes. When such agents are used, exposure to radiation results only from the X-ray equipment used in the examination. The chemical structure of radiopaque contrast agents can produce a variety of adverse reactions, some of which may be severe and possibly life-threatening in certain individuals.

213. **RADIOPHARMACEUTICALS** - Drugs (compounds or materials) that may be labeled or tagged with a radioisotope. These materials are largely physiological or subpharmacological 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.

214. **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.

215. **RECOMBINANT DNA TECHNOLOGY** - "The ability to chop up DNA, the stuff of which genes are made, and move the pieces, [which] permits the direct examination of the human genome," and the identification of the genetic components of a wide variety of disorders [Holtzman (1989), p. 1]. Recombinant DNA technology is also used to develop diagnostic screens and tests, as well as drugs and biologics for treating diseases with genetic components.

216. **RECUSAL** – The temporary absence of the IRB member during deliberation and vote on the project with respect to which the member has a conflict.

217. **REM (ROENTGEN EQUIVALENT IN MAN)** - the unit of measurement for a dose of an ionizing radiation that produces the same biological effect as a unit of absorbed does (1 rad) of ordinary X-rays. One millirem is equal to 1/1000 of a rem.

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

219. **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.)

220. **REPOSITORY** – A common site for storage of collection of human biologic specimens available for study. This may be one geographic location or may be a virtual aggregation of biologic specimens from many locations. Repositories are also referred to as tissue banks, collection, resources, inventories, or by other terms. Repository activities involve three components: (i) the **collectors** of tissue samples; (ii) the **repository** storage and data management center; and (iii) the **recipient.**

221. **RESEARCH**

a) **(as defined by DHHS regulations) [45 CFR 46.102(l)].** – A systematic investigation, including research development, testing and evaluation designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

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

(ii) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing

timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(iii) Collection and analysis of information, biospecimens, or records by or for a criminal justice or criminal investigative purposes.

(iv) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

b) **(as defined by FDA regulations)** *(synonymous with the term* **Clinical Investigation**)

(1) Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of Part 58 of 21 CFR 58 ("Good Laboratory Practice for Nonclinical Laboratory Studies"). The terms ***research*****,** ***clinical research*****,** ***clinical study*****,** ***study*****,** and ***clinical investigation*** are deemed to be synonymous. [21 CFR 50.3(c) and 21 CFR 56.102(c)]

(2) Any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. An experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. [21CFE 312.3(b)]

(3) **Investigation** means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

222. **RESEARCH CERTIFICATES OF CONFIDENTIALITY** – Situations where the Investigator requires protection of research of a sensitive nature and the Principal Investigator has applied to the Department of Health and Human Services to protect this information. This allows a researcher to protect the privacy of research subjects by withholding from most persons not connected with the research team the names and other identifying information relating to research subjects. The protection will be granted only when the

research is of a sensitive nature where the protection is judged necessary to achieve the research objectives. Examples include research relating to sexual attitudes, preferences, or practices, the use of alcohol, drugs, or other addictive products, pertaining to illegal conduct or to an individual's psychological well being or mental health, genetic information, information that, if released, could be damaging to an individual's financial standing, employability, or reputation, and information that would normally be recorded in a patient's medical record that, if released, could lead to social stigmatization or discrimination. Researchers may receive a Certificate of Confidentiality regardless of funding source. Researchers who receive a certificate may not be compelled by Federal, State or local legal processes or subpoenas to disclose information that they possess as a consequence of the research.

223. **RESEARCH MISCONDUCT** – Intentional, reckless or negligent failure to abide by applicable law, regulations, or IRB procedures; plagiarism; fabrication or intentional falsification of data, research procedures or data analysis; or other deliberate misrepresentation in proposing, conducting, reporting, or reviewing research. It does not include honest error or honest differences in interpretations or judgments of data. In cases of allegations involving activities submitted to or supported by a federal agency, the definition for misconduct specified in the agency's regulations will apply.

224. **RESPECT FOR PERSONS** - An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

225. **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.

226. **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.

227. **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.)

228. **SAMHSA SUBSTANCE ABUSE AND MENTAL HEALTH SERVICES ADMINISTRATION -** includes the Center for Substance Abuse Prevention, the Center for Substance Abuse Treatment and the Center on Mental Health Services. Previously the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA). (See also: ADAMHA.)

229. **SAMPLE** – In context of this policy, a sample refers to any human biological material. This includes, but is not limited to, molecular material such as DNA, cells tissue (blood, bone, muscle, etc), organs (liver, bladder, heart, etc) gametes, embryos, fetal tissue, waster (hair, nail clippings, urine, feces, saliva, sputum, etc) and other materials of human origin.

230. **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).

231. **SECRETARY** - A U.S. Cabinet Officer. In the context of DHHS-conducted or -supported research, usually refers to the Secretary of Health and Human Services.

232. **SENSITIVE INFORMATION** - includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information relating to illegal conduct; information that if released, might be damaging to an individual's financial standing, employability, or reputation in the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples (NIH, Frequently Asked Questions on Certificates of Confidentiality, March, 2002).

233. **SERIOUS NONCOMPLIANCE** – knowingly disregarding or violating federal regulations or institutional policies and procedures applicable to human subjects research, which, in the judgment of the IRB, could place subjects at risk of significant harm. For VA research, serious non-compliance is a failure to adhere to the laws, regulations, or policies governing research involving human subjects that may reasonably be regarded as: 1) involving substantive harm, or a genuine risk of substantive harm, to the

safety, rights, or welfare of human research subjects, research staff, or others and/or 2) substantively compromising the effectiveness of a VA facility's HRPP. In all cases, the determination that non-compliance is serious rests with the IRB.

234. **SERIOUS UNANTICIPATED PROBLEM (SAE)** – Any event that results in death, a life-threatening situation, hospitalization or prolonged hospitalization, persistent or significant disability/incapacity or a congenital anomaly/birth defect or requires medical intervention to prevent one of the outcomes listed above. SAEs require prompt reporting to the Sponsor, the FDA and the IRB.

235. **SEVERELY DEBILITATING** - diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke (FDA Information Sheet, 1998).

236. **SIGNIFICANT COMPLAINTS, ISSUES OR CONCERNS -** problems that relate to subjects' safety, rights, and/or welfare.

237. **SIGNIFICANT FINANCIAL CONFLICT OF INTEREST** is aligned with the guidelines of the Public Health Service and exists when any member of a research team or his/her immediate family receives or is likely to receive direct, personal remuneration of at least $10,000 from or holds a 5% or greater ownership in a company involved in research, training, patient care and/or administrative activities related to the sponsored project.

238. **SIGNIFICANT RISK DEVICE** or **SIGNIFICANT RISK INVESTIGATIONAL DEVICE** - An investigational medical device that a potential for serious risk to the health, safety, or welfare of a subject and a) is intended as an implant, or b) used in supporting or sustaining life, or c) is of substantial importance in diagnosing, curing, mitigating, or curing disease, or otherwise prevents impairment of human health, or d) otherwise prevents a potential for serious risk to the health, safety, or welfare of a subject [21 CFR 812.3(m)].

239. **SIGNIFICANT RISK (SR) DEVICE STUDY** – A study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and
    a) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant;
    b) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a participant;

c) Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of a participant; or

d) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

240. **SINGLE-BLIND OR 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.

241. **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.

242. **SOCIAL EXPERIMENTATION** - Systematic manipulation of, or experimentation in, social or economic systems; used in planning public policy.

243. **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. A clinical 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. [21 CFR 312.3(b)]

244. **SPONSOR-IMPOSED HOLD** – A sponsor-initiated action to place all or some specific research activities on hold. This decision may be made from interim data analysis, inadequate drug stocks, response to a DSMB report; or a preplanned stopping point. This may also occur as a result of new information potentially altering participants' risk/benefit ratio.

245. **SPONSOR-INVESTIGATOR** - an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The

requirements applicable to a sponsor-investigator under this part [21 CFR 312 Subpart D] include both those applicable to an investigator and a sponsor. [21 CFR 312.3(b)].

246. **SPONSORED RESEARCH** – Research that is commercially funded by a business enterprise (e.g., pharmaceutical company or device manufacturer); government sponsored research and/or private sponsored research.

247. **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. [See McLarty (1987), p. 2.] 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).

248. **STERILITY**
    a) The absence of viable contaminating microorganisms; aseptic state.
    b) The inability to procreate; the inability to conceive or induce conception.

249. **STUDY SECTION** - See: Scientific Review Group.

250. **STUDY STAFF** – Research nurses and study coordinators that are involved in the research process, including but not limited to, patient recruitment, patient care, data collection and records completion.

251. **SUBJECTS (HUMAN)** - See: Human Subjects.

252. **SUBSTANTIVE CHANGES** - Non-minor changes that significantly alter the study design, study population and/or risks.

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

254. **SUSPENSION OF IRB APPROVAL** – The IRB Board may direct a Principal Investigator and his/her colleagues to cease enrollment and/or to cease all or part of study procedures in the interest of subject safety. This may, upon direction of the board, become a full study termination. With corrective action on the part of the Principal Investigator the full board may withdraw study suspension, returning the study to full active status. Under emergency circumstances, this decision may be made by the Chair, Vice-Chair or ORI Director.

255. **SYSTEMATIC INVESTIGATION** – A planned and orderly process through which a hypothesis or research questions is formulated, data are collected and analyzed, and results are interpreted in terms of the hypothesis or research question.

256. **TECHNOLOGY** – Any compound, drug, device, diagnostic, medical or surgical procedure intended for use in health care delivery.

257. **TERMINATION OF IRB APPROVAL** – The IRB may direct a Principal Investigator and his/her colleagues to cease enrollment and all other study procedures in the interest of subject safety. The IRB will notify the Principal Investigator that all currently enrolled subjects must be notified of study termination and given recommendations of clinical treatment, as appropriate. Under emergency circumstances, this decision may be made by the Chair, Vice-Chair or ORI Director.

258. **TEST ARTICLE** – A drug or device that is being tested for safety and effectiveness, not yet approved by the FDA for general use, or not yet approved for the particular use being researched.

259. **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.) 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.

260. **THERAPY** - Treatment intended and expected to alleviate a disease or disorder.

261. **UNANTICIPATED PROBLEM** – Any unplanned occurrence that may affect the risks and/or potential benefits involved in the research study. Unplanned occurrences are usually related to study design or methods. Such occurrences can be favorable or unfavorable to participants and may or may not influence the study objectives or results (e.g., loss of confidentiality).

262. **UNEXPECTED UNANTICIPATED PROBLEM (UAE)** – Any problem that was unanticipated or not previously observed (e.g., not included in the consent form or investigator brochure). This includes adverse events that occur more frequently or with greater severity than anticipated. Events that are unexpected and serious require prompt reporting to the Sponsor, the FDA and the IRB.

263. **UNAPPROVED DEVICE** - A device that is used for a purpose or condition for which the device requires, but does not have an approved application for pre-market approval under section 515 FD&C Act & [21 United States Code (USC) chapter 9, subchapter IV, § 360(e)]. An unapproved device may be used in human subjects only if approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under the FDCA [21USC ch9, subch. IV § 360(j)(g) and [21CFR part 812.] Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices.

264. **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.

265. **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.

266. **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.

267. **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 [45 CFR 46.203(d)]. 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 [Federal Register 40 (August 8, 1975): 33552]. These indices depend on the state of present technology and may be revised periodically. (See also: Nonviable Fetus.)

268. **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.

269. **VULNERABLE SUBJECTS/PARTICIPATION** – Individuals who lack the capacity to provide informed consent or whose willingness

to participate in research may be subject to undue influence or coercion. Vulnerable subjects include, for example, children, prisoners, individuals with emotional or cognitive disorders/impairments and economically or educationally disadvantaged persons.

270. **WAIVER OF HIPAA AUTHORIZATION** – Documented HIPAA permitted waiver of authorization when an IRB reviews the request according to the required criteria.

271. **WAIVER OR ALTERATION OF REQUIRED ELEMENTS OF CONSENT** - An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent. HHS CFR 45.46.116(e)

272. **WAIVER OF WRITTEN DOCUMENTATION OF INFORMED CONSENT** - An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds:

    a) that the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research. : HHS CFR 45.46.117(c)(1)

    b) that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (e.g. telephone survey). In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research. If requesting a waiver of documentation of informed consent, provide the script or information sheet that will be used. HHS CFR 45.46.117(c)(2)

273. **WARD OF THE STATE** – Person who, because of age or infirmity or by statue put under the protection of the state which supports the person and makes decisions for them. Commonly used with minor children, abused elderly person, and prisoners.

274. **WITNESS** - an individual 18+ years of age who observes the subject signing the informed consent document. When authorized by the IRB, a short form written consent document stating the elements of informed consent can be presented orally. When this method is used, the witness signature verifies s/he was present to the oral presentation.