

APPENDIX K

DEFINITIONS

ANONYMITY- Anonymity exists when there are no identifiers on project materials which could link the data with individual subjects. Even the research investigator cannot know the identity of participants.

ASSENT - Agreement to participate in proposed research, given by an individual not competent to give legally valid informed consent (e.g., a child or mentally limited person). Mere failure to object may not be construed as assent.

ASSURANCE - A formal, written statement submitted to a federal agency attesting that an institution will comply with applicable rules governing research with human subjects.

BENEFIT - A valued or desired outcome. An advantage.

BID - Twice a day.

BIOLOGIC - Any virus, therapeutic serum, toxin, antitoxin or analogous product used for the prevention, treatment or cure of diseases or injuries of humans.

CHILDREN - Those who have not attained the legal age for consent (<18).

CLASS I, II, III DEVICES - Classification by the FDA of medical devices according to degree of potential risks or hazards.

CLINICAL TRIAL: A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of an investigational drug or device. Clinical trials are typically conducted by investigators who have entered into an agreement with a sponsor to conduct the study. For clinical drug and device trials, investigators agree to conditions regarding the conduct of the study outlined by Food and Drug Administration (FDA). Clinical trial investigators agree to these conditions by signing a FDA form (FDA Form 1572) that certifies that the investigator has obtained IRB review and approval prior to conducting the study.

CODE OF FEDERAL REGULATIONS (CFR) - A compendium of rules issued by federal agencies on a multiplicity of topics.

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

COMPENSATION - Payment or medical care provided to subjects injured in research. Does not refer to payments (remuneration) for participation in research.

COMPETENCE - Technically, a legal term used to denote capacity to act on one's own behalf. The ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Competence may fluctuate as a function of the natural course of a mental illness, response to treatment, effects of medication, general physical health and other factors. Therefore, mental status should be reevaluated periodically. As a designation of legal status, competence or incompetence pertains to an adjudication in court proceedings that a person's abilities are so diminished that his or her decisions or actions (e.g., writing a will) should have no legal effect. Such adjudications are often determined by inability to manage business or monetary affairs and do not necessarily reflect a person's ability to function in other situations.

CONFIDENTIALITY - Right of privacy and of nonrelease of disclosed personal information. The investigator should protect subjects against invasion of privacy and loss of confidentiality. Lack of secure handling of completed personality tests, questionnaires, interview protocols or data and recorded materials augments risk and must be avoided.

CONTROL - Subjects who are not given a treatment under study or do not have a given disorder, background or risk that is the object of study, and who are comparable to subjects in the study.

CROSSOVER DESIGN - A type of clinical trial in which each subject is given, at different times, both an experimental and a control therapy.

DATA POINTS - Any text or numbers generated during a study.

DOUBLE-BLIND DESIGN - A study comparing two or more treatments in which neither the investigators nor the subjects know to which treatment group individual subjects have been assigned.

EMANCIPATED MINOR - A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities such as self-support, marriage or procreation.

EXPERIMENTAL - A term often used to denote a therapy (drug, device or procedure) that is unproven or scientifically unvalidated with respect to safety and efficacy. A procedure may be considered "experimental" without necessarily being part of a formal study to evaluate its usefulness.

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

FETUS - The product of conception from the time of implantation until a determination is made, following expulsion or extraction, that it is viable. The term "fetus" generally refers to later phases of development. The term "embryo" is usually used for earlier phases of development.

GROUP C TREATMENT IND: "Group C" Treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means by which oncologists can use investigational drugs for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase III study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected.

GUARDIAN - A person who is authorized by law to consent on behalf of a child or handicapped individuals to general medical care.

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. (Note: the condition of subjects may be compared with their own condition on a prior regimen, the effectiveness of which has already been established.)

HUMAN SUBJECT - Under DHHS regulations human subjects are living individuals about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual or 2) identifiable private information. Intervention includes both the physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact (e.g., questionnaires, interviews) between the investigator and the subject (45 CFR 46.102). 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.

Under FDA regulations a human subject is defined as "an individual who is or becomes a participant in research, either as a recipient of a test article or as a control (21 CFR 50.03, 21 CFR §56.103(e), 21 CFR §312.3(b)). A subject may be either a healthy individual or a patient." If the research involves a medical device, human subjects are individuals when they participate in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control (21 CFR §812.3(p)).

HUMAN SUBJECT RESEARCH – Under the Organization's policies and procedures an activity is human subject research if it is either (1) human research subject to FDA regulation or (2) human research subject to DHHS regulations. Activities are human research subject to FDA regulations when they meet the FDA definition of "research" and involve one or more "human subjects" as defined in FDA regulations. Activities are human research subject to DHHS regulations when they meet the DHHS definition of "research" and involve one more "human subjects" as defined in DHHS regulations (§46.102(f))

HUMAN IN VITRO FERTILIZATION - Any fertilization involving human sperm and ova that occurs outside the human body. **INCAPACITY** - Refers to a person's mental status and means inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information and to make a choice. Often used as a synonym for incompetence.

INCOMPETENCE - Legally, the inability to manage one's affairs. Often used as a synonym for incapacity.

INFANT - An ex utero fetus judged viable (i.e., likely to survive to the point of sustaining life independently).

INFORMED CONSENT - Informed consent means "knowing consent," the exercise of a free power of choice without undue inducement, force, fraud, deceit, duress or other form of constraint or coercion. If the subjects are minors or are not capable of giving consent, parental, guardian or other legal representative consent is required. Use of a written consent form that includes all of the basic elements of informed consent must be documented by a signature of the subject or legally authorized representative.

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

INTERACTION - Interaction includes communication or interpersonal contact between investigator and subject.

INTERVENTION - "Intervention" includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

INVESTIGATIONAL DEVICE - A medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device.

INVESTIGATIONAL NEW DRUG (IND) - A drug permitted by the FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population, and thus, not yet licensed for marketing.

INVESTIGATIONAL DEVICE EXEMPTION (IDE) - An exemption from certain rules found in the Medical Device Amendments, allowing use of a not-yet-approved devices in clinical investigators.

INVESTIGATOR - Clinician responsible for conducting the study.

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

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

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

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.

MEDICAL DEVICES - Diagnostic or therapeutic articles that do not interact chemically with the body. Such devices may include diagnostic test kits, crutches, electrodes, prescribed beds, pacemakers, arterial grafts, intraocular lenses and orthopedic pins.

MINIMAL RISK - 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.

MONITOR - Designated individual selected by a sponsor or contract research organization to oversee the progress of a clinical investigation.

NONSIGNIFICANT RISK DEVICE - An investigational medical device that does not present significant risk as described above. The determination that a device presents a nonsignificant risk is first made by the sponsor. If the IRB agrees with the sponsor's finding that a device presents nonsignificant risk, the device is considered a nonsignificant risk device.

NORMAL SUBJECT - Subjects used in study of normal physiology and behavior, or subjects who do not have the condition under study in a particular protocol used as comparisons with subjects who do have the condition. "Normal" does not necessarily connote normal in all respects. For example, patients with broken legs may serve as normal volunteers in studies of metabolism, cognitive development and the like. Similarly, patients with heart disease but without diabetes may be "normals" in a study of diabetes complicated by heart disease.

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

PARALLEL TRACK IND: The FDA's Parallel Track policy permits wider access to new drugs for life-threatening diseases under a separate treatment protocol (Parallel Track IND) that "parallels" the controlled Phase II and III clinical trials performed to establish the safety and effectiveness of investigational new drugs. For example, under this prospective mechanism, persons with AIDS and HIV-related diseases who are not able to take standard therapy or for whom standard therapy is no longer effective, and who are not able to participate in ongoing controlled clinical trials, can have access to promising investigational new drugs. Applications to permit expanded availability of an investigational new drug under the Parallel Track mechanism must be submitted (typically by the manufacturer of the drug) to the FDA as an amendment to the existing IND.

PARENT - A child's biological or adoptive parent.

PERMISSION - The agreement of the parent(s) or guardian to the participation of the child, handicapped individual, or ward in the research.

PHASE I (CLINICAL) TRIAL - The first stage in testing an unapproved (by the FDA) drug in man. The drug is administered to a small number of normal subjects to generate preliminary information on its safe dosage, toxicity, tolerance, absorption and metabolism. However, in some instances, if the drug is intended to treat a specific disease, it may be appropriate to test the drug in patients with that disease.

PHASE II (CLINICAL) TRIAL - The second stage in testing a new drug in man, generally carried out on patients with the disease or condition of interest to obtain information on the treatment efficacy and to supplement information on safety obtained from Phase I trial.

PHASE III (CLINICAL) TRIAL - The third, and usually final stage in testing a drug in man. The study is designed to include a control treatment and random allocation to treatment on a large subject population in different clinical settings. The drug is used as would be when marketed and the study is primarily concerned with assessments of dosage effects and efficacy and safety. Once this phase is completed, the drug manufacturers may request permission to market the drug by submission of a New Drug Application to the FDA.

PHASE IV (CLINICAL) TRIAL - Generally carried out after FDA approval and licensure of the drug for that indication. The study is a randomized controlled trial designed to evaluate the long-term safety and efficacy of a drug for the given information.

PHLEBOTOMIST - An individual trained to draw blood.

PHYSICAL RISK - Any strenuous or unusual physical activity or procedure required of a subject, use of compounds which might alter the subject's biochemical milieu, exposure to strong stimulation or placement in a situation which could lead to violence. The investigator is responsible for anticipating circumstances which might endanger the subject's physical well-being and for bringing these circumstances to the attention of the IRB.

PHYSIOLOGICAL RISK - Any experimental condition that induces personality change or intense changes in a subject's feelings or motivations, or that may induce such changes which extend beyond the experimental or debriefing period. Subjection to deceit, to demeaning or dehumanizing procedures, to humiliation and embarrassment. The investigator has the responsibility to eliminate or minimize the effects of psychological risk to subjects and to bring these matters to the attention of the IRB.

PREGNANCY - The period from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (i.e., has been delivered). 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.

PRISONER - An individual involuntarily confined in a penal institution, including persons (a) sentenced under a criminal or civil statute, (b) detained pending arraignment, trial or sentencing, and © 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 penal institution [45 CFR 46.303(c)]. **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 (e.g., 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.

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

PROTOCOL - A protocol is the researcher's plan of a scientific experiment or treatment. Full review or expedited protocol consists of a cover sheet, Unit/Department/Faculty Review form, Human Subjects Protocol Form, informed consent form(s), sample survey instrument(s) or questionnaire(s), and grant proposal, thesis or dissertation, or prospectus, so as to provide complete information regarding activities involving human subjects. Claim of Exemption from IRB forms are also available.

QUALITY ASSURANCE - A system of activities whose purpose is to provide assurance that the overall control of quality is being done effectively.

RADIOPHARMACEUTICALS - Drugs, compounds, or materials labeled or tagged with a radioisotope. These materials are largely physiological in action and, in many cases, function much like materials found in the body. The principal risk associated with these materials is the radiation exposure to the body or to specific organ systems when they are injected in the body.

RANDOMIZATION OR RANDOMIZED CLINICAL TRIALS - Assignment of subjects to different treatments, interventions or conditions according to chance rather than with reference to some aspect of their condition, history or prognosis.

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

Under FDA Regulations (21 CFR 56.102) the term "clinical investigation" is synonymous with "research" and is defined as "any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Food, Drug and Cosmetic Act, or need not

meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. Clinical investigations regulated by the FDA under Sections 505(i) and 520(g) of the Act, include investigations of food, dietary supplements that bear a nutrient content claim or a health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. The term "clinical investigation" does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.

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

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

RISK - 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.")

SIGNIFICANT RISK DEVICE - An investigational medical device that: 1) Is intended as an implant and presents a potential for serious risk to the health, safety or welfare of a subject; 2) Is purported or represented to be of use in supporting or sustaining human life and presents a potential for serious risk to the health, safety or welfare of a subject; 3) Is for a use of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health, and which presents a potential for serious risk to the health, safety or welfare of a subject; 4) Otherwise presents a potential for serious risk to the health, safety or welfare of a subject; or 5) Other than minimal risk

SINGLE-BLIND DESIGN - Typically, a study designed in which the investigator, but not the subject, knows the treatment assignment. Occasionally the subject, rather than the investigator, knows the assignment.

SPONSOR (of a drug trial) - The developer of a new drug who distributes it to investigators and physicians for clinical trials, and who is responsible for securing FDA clearance for trials and form reporting the results of those trials to the FDA. A sponsor may be either a private pharmaceutical manufacturer, a research institute, a clinical investigator or a federal agency.

SPONSOR - The company/person who initiates the study. The sponsor is typically the manufacturer or research institute that developed the drug or device. In this case, the sponsor does not actually conduct the clinical trial but rather distributes the investigational drug or device to

clinical investigators who direct local conduct of the trial. A clinical investigator may, however, serve as both the sponsor and investigator (investigator-sponsor) of a clinical trial. The sponsor assumes general responsibility for the studies involving the investigational drug or device, including responsibility for compliance with applicable laws and regulations. The sponsor is responsible for obtaining FDA approval to conduct a trial and for reporting the results of the trial to the FDA.

STUDY COORDINATOR - Person appointed at the institute/center where the study is being conducted.

SUBJECT - A non-patient (normal) volunteer or a patient in clinical research.

TERMINALLY ILL - Terminally ill patients are those who are deteriorating from a life-threatening disease or condition for which no effective standard treatment exists.

THERAPEUTIC RESEARCH - Research involving an intervention that has the likelihood of providing a therapeutic, diagnostic or preventive benefit to the subjects.

THERAPEUTIC INTENT - The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinking of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected). This term is sometimes associated with Phase I drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some improvement in the patient's condition, as well as assessing the safety and pharmacology of a drug.

TID - Three times a day.

TREATMENT IND: Established by the FDA in 1987, a Treatment Investigational New Drug exemption (Treatment IND) is a treatment protocol that is added to an existing IND for a promising new investigational drug. The Treatment IND provides a prospective mechanism whereby physicians can treat multiple, eligible patients with the investigational new drug according to protocol. A Treatment IND may be granted by the FDA (i.e., typically to the drug manufacturer, but also to investigator-sponsors) after sufficient data have been collected to show that the drug may be effective and does not have unreasonable risks. Because data related to safety and side effects are collected, Treatment INDs also serve to expand the body of knowledge about the investigational new drug. There are four requirements that must be met before a Treatment IND can be issued by the FDA: a) the drug is intended to treat a serious or immediately life-threatening disease; b) there is no satisfactory alternative treatment available; c) the drug is already under investigation, or trials have been completed; and d) the sponsor of the drug is actively pursuing its market approval.

TREATMENT AND PARALLEL TRACK INDs: Investigational new drugs may be made available outside of a clinical trial, through a treatment protocol, to multiple patients with life-threatening or other serious diseases for which no satisfactory alternative drug or other therapy exists. (For information related to the emergency use of an unapproved drug or device in a single patient, refer to section 2.4 of this IRB Reference Manual.)

UNANTICIPATED: Unforeseeable at the time of its occurrence.

UNANTICIPATED PROBLEM INVOLVING RISKS TO HUMAN SUBJECTS OR OTHERS: Any problem or event that, in the opinion of the principal investigator 1) was unanticipated; 2) involved risk to human subjects or others e.g., research staff, family members, University IRB Office staff, University or UPMC), and 3) was related to a research intervention.

UNEXPECTED: Not identified by nature, severity or frequency in the current University IRB-approved research protocol or informed consent document.