

Institutional Review Board Guidebook

This is the complete glossary from the IRB Guidebook on the OHRP website, along with a short description of the guidebook contents . Link to the IRB Guidebook at http://www.hhs.gov/ohrp/irb/irb_preface.htm.

HOW TO USE THE GUIDEBOOK

The Guidebook is divided into the following chapters:

Introduction. Provides a basic understanding of the background and purposes of the IRB review system. It should be particularly useful for new IRB members and investigators just beginning their clinical research. The Introduction includes a description of **The Belmont Report**, providing a summary of the principles set forth in this seminal policy statement on the protection of human subjects of research.

[Chapter 1.](#)

Institutional Administration. Directed primarily at institutional administrators and IRB chairpersons. It will also be of interest to others on the IRB, clinical investigators, and sponsors of research who wish to consider how the IRB relates to other institutional offices.

[Chapter 2.](#)

Regulations and Policies. Assists in resolving uncertainties about the intent or interpretation of regulatory provisions. It should also be a useful reference for initial reviewers of research proposals.

[Chapter 3.](#)

Basic IRB Review. Presents the major focal points of IRB review: informed consent, risk/benefit analysis, privacy and confidentiality, selection of subjects, and incentives for participation. It goes beyond the regulations in suggesting how the regulations might be applied in various situations.

[Chapter 4.](#)

Considerations of Research Design. Provides descriptions of, and information on, the reasons for using certain experimental designs. The ethical issues raised by such uses are also explored.

[Chapter 5.](#)

Biomedical and Behavioral Research: An Overview. Describes certain kinds of research by subject matter and their various goals and methods in a general, introductory way, pointing out the ethical concerns each raises and providing references for further reading. This chapter will be of most benefit to nonscientists on the IRB and to scientist-reviewers confronting a research proposal in an unfamiliar discipline.

[Chapter 6.](#)

Special Classes of Subjects. Provides an analysis of the ethical issues that arise in research involving classes of particularly vulnerable research subjects. Regulations exist for some classes of subjects; for others, no regulations are in place.

Institutional Review Board Guidebook

* GLOSSARY *

GLOSSARY OF TERMS

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

ADAMHA Alcohol, Drug Abuse, and Mental Health Administration; reorganized in October 1992 as the Substance Abuse and Mental Health Services Administration (SAMHSA). ADAMHA included the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), the Office for Substance Abuse Prevention (OSAP), and the Office for Treatment Intervention (OTI). NIMH, NIAAA, and NIDA are now part of the National Institutes of Health (NIH). (*See also: SAMHSA.*)

ADJUVANT THERAPY Therapy provided to enhance the effect of an primary therapy; auxiliary therapy.

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).

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

ASSURANCE A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved [Federal Policy ?___.103].

AUTHORIZED INSTITUTIONAL OFFICIAL An officer of an institution with the authority to speak for and legally commit the institution to adherence to the requirements of the federal regulations regarding the involvement of human subjects in biomedical and behavioral research.

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

AUTOPSY Examination by dissection of the body of an individual to determine cause of death and other medically relevant facts.

BELMONT REPORT A statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

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

BENEFIT A valued or desired outcome; an advantage.

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

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

CADAVER The body of a deceased person.

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.*)

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

CHILDREN Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.401(a)].

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

CLASS I, II, III DEVICES Classification by the Food and Drug Administration of medical devices according to potential risks or hazards.

CLINICAL TRIAL A controlled study involving human subjects, designed to evaluate prospectively the safety and effectiveness of new drugs or devices or of behavioral interventions.

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

COHORT A group of subjects initially identified as having one or more characteristics in common who are followed over time. In social science research, this term may refer to any group of persons who are born at about the same time and share common historical or cultural experiences.

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

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

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

CONSENT *See: Informed Consent.*

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.*)

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.

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).

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.

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

DATA AND SAFETY MONITORING BOARD 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.

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.

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.)

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.

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).

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

DEVICE (MEDICAL) *See: Medical Device.*

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.

DHHS A federal agency: U.S. Department of Health and Human Services; formerly the Department of Health, Education and Welfare (DHEW).

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

DOUBLE-MASKED DESIGN A study design in which neither the investigators nor the subjects know the treatment group assignments of individual subjects. Sometimes referred to as "double-blind."

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.

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.*)

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.*)

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

EQUITABLE Fair or just; used in the context of selection of subjects to indicate that the benefits and burdens of research are fairly distributed [Federal Policy ?____.111(a)(3)].

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.

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.*)

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.

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 [Federal Policy ?____.110].

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.*)

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.*)

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).

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).

FDA 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.

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.")

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

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

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.*)

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."

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 [Federal Policy ?____.108].

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

GENERAL ASSURANCE Obsolete term, previously used to denote an institutional assurance covering multiple research projects. (*See also: Assurance.*)

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)].

GENETIC SCREENING Tests to identify persons who have an inherited predisposition to a certain phenotype or who are at risk of producing offspring with inherited diseases or disorders.

GENOTYPE The genetic constitution of an individual.

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.*)

GUARDIAN An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care [45 CFR 46.402(3)].

HELSINKI DECLARATION *See: Declaration of Helsinki.*

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.

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

HUMAN SUBJECTS Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as: living individual(s) about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information [Federal Policy ?____.102(f)].

IDE *See: Investigational Device Exemptions.*

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.*)

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

IND See: Investigational New Drug.

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

INFORMED CONSENT A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence [Federal Policy ?116; 21 CFR 50.20 and 50.25].

INSTITUTION (1) Any public or private entity or agency (including federal, state, and local agencies) [Federal Policy ?__.102(b)].

INSTITUTION (2) A residential facility that provides food, shelter, and professional services (including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care). Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

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 [Federal Policy ??__.102(g), ____.108, ____.109].

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

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).

INVESTIGATIONAL DEVICE EXEMPTIONS (IDE) Exemptions from certain regulations found in the Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations [21 CFR 812.20].

INVESTIGATIONAL NEW DRUG OR DEVICE A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

INVESTIGATOR 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.*)

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*.

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*).

IRB See: *Institutional Review Board*.

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.

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

LEGALLY AUTHORIZED REPRESENTATIVE 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 [Federal Policy ? ____.102(c)].

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

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

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-Masked Design; Single-Masked Design.*)

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.*)

MEDICAL DEVICE A diagnostic or therapeutic article that does not achieve any of its principal intended purpose through chemical action within or on the body. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intraocular lenses, and orthopedic pins or other orthopedic equipment.

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.

MENTALLY DISABLED *See: Cognitively Impaired.*

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.

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 [Federal Policy ? ____.102(i)]. 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.

The definition of minimal risk for research involving prisoners differs somewhat from that given for noninstitutionalized adults. [*See 45 CFR 46.303(d) and Guidebook Chapter 6, Section E, "Prisoners."*]

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

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.

NDA *See: New Drug Application.*

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

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

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

NIH National Institutes of Health: a federal agency within the Public Health Service, DHHS, comprising 21 institutes and centers. It is responsible for carrying out and supporting biomedical and behavioral research.

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

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).

NONSIGNIFICANT RISK DEVICE An investigational medical device that does not present significant risk to the patient. (*See also: Significant Risk Device.*)

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.

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.*)

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

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

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

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.

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

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

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

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

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

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).

- **PHASE 1 DRUG TRIAL** Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; sometimes, where the drug is intended for use in patients with a particular disease, however, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness; they are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. The total number of subjects involved in Phase 1 investigations is generally in the range of 20-80.
- **PHASE 2 DRUG TRIAL** Phase 2 trials include controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well-controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects.
- **PHASE 3 DRUG TRIAL** Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide 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.

- **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].

PHENOTYPE The physical manifestation of a gene function.

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

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

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

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

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

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

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.

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

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.

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

PRISONER An individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (*e.g.*, for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution [45 CFR 46.303(c)].

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

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.

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

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.

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.

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.

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.*)

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

RADIOACTIVE DRUG RESEARCH COMMITTEE (RDRC) An institutional committee responsible for the use of radioactive drugs in human subjects for research purposes. Research involving human subjects that proposes to use radioactive drugs must meet various FDA requirements, including limitations on the pharmacological dose and the radiation dose. Furthermore, the exposure to radiation must be justified by the quality of the study and the importance of the information it seeks to obtain. The committee is also responsible for continuing review of the drug use to ensure that the research continues to comply with FDA requirements, including reporting obligations. The committee must include experts in nuclear medicine and the use of radioactive drugs, as well as other medical and scientific members [21 CFR 36.1].

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.

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.

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.

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. See Guidebook Chapter 5, Section H, "Human Genetic Research."

REM Acronym for 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 dose (1 rad) of ordinary X-rays. One millirem is equal to 1/1000 of a rem.

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.

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.*)

RESEARCH A systematic investigation (*i.e.*, the gathering and analysis of information) designed to develop or contribute to generalizable knowledge [Federal Policy § 102(d)].

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.

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.

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 [Federal Policy § 108(e)].

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.*)

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.*)

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).

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.

SIGNIFICANT RISK DEVICE An investigational medical device that presents a potential for serious risk to the health, safety, or welfare of the subject.

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

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.

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

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.

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

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).

STERILITY (1) The absence of viable contaminating microorganisms; aseptic state.

STERILITY (2) The inability to procreate; the inability to conceive or induce conception.

STUDY SECTION *See: Scientific Review Group.*

SUBJECTS (HUMAN) *See: Human Subjects.*

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

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.

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

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.

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.

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.

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.*)

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.

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