

GLOSSARY

Acronyms

FR – Code of Federal Regulations

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

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.

HIC – Human Investigation Committee: the name of the institutional review board for Wayne State University and its affiliated health care institutions (i.e., Barbara Ann Karmanos Cancer Institute, Children’s Hospital of Michigan, Detroit Receiving Hospital/University Health Center, Sinai-Grace Hospital, Harper University Hospital, Hutzel Women’s Hospital, Huron Valley/Sinai Hospital, Rehabilitation Institute of Michigan, John D. Dingell Veterans Administration Medical Center, and the Michigan Orthopedic Surgery Hospital).

IRB – Institutional Review Board (see definition below)

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

OHRP – Office for Human Research Protection (see definition below)

Definitions

Administrative Hold – a temporary hold on the ability of a principal investigator to enroll new human subjects on a research protocol until the Human Investigation Committee has determined that adequate safeguards for the protection of human subjects have been developed.

Adverse Event – 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).

Adverse Reaction (AR): an undesirable and unintended, although not necessarily unexpected, result of therapy, study interventions or activities. Adverse reactions generally occur in clinical research and only apply to participants enrolled in the research study. Some examples of Adverse Reactions include: (1) Allergic reaction to a study drug, (2) Failure of an implanted experimental device, (3) Headache following spinal tap, (4) Intestinal bleeding

associated with aspirin therapy, (5) Discomfort of the participant during a research interview and Death.

Anonymous Samples - specimens obtained by an investigator without any identifying information and without a link to a specific individual.

Approval - the full IRB Committee, IRB Chairperson, HIC Chairperson or his/her designee has approved the research protocol, for a period not to exceed one year.

Adverse Reaction/Unexpected Event (AR/UE) Report - a report that is generated from the specific reports submitted by the PI to the HIC, the findings and recommendations of the AR/UE reviewer and any follow-up responses from the PI. This report is presented to all IRB members for their review, discussion and vote at each convened meeting.

Assent – affirmative agreement by an individual not competent to give legally valid informed consent to participate in research (e.g., a child or cognitively impaired person). Mere absence of an objection should not be construed as assent.

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.

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.

Children (Minor) – persons who are less than 18 years of age. In Michigan the legal age for consent is 18 years of age. “Minors” are defined as “persons less than 18 years of age;” and therefore, are considered “children” for purposes of the regulations pursuant to Michigan State Law (See Michigan Compiled Laws Annotated [MCLA] 722.1).

Clinical Investigation - any experiment that involves a test article (in this case, a drug or biological drug) and one or more human subjects (participants) and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by the FDA as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of part 58, regarding non-clinical laboratory studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous for purposes of this part.” [21 CFR 56.102(c)].

Clinical Investigator - according to the Food and Drug Administration (FDA), a clinical investigator is defined as “an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed or used involving a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team” [21 CFR 56.102(h)].

Clinical Personnel – persons who are members of the clinician's staff who have a legitimate reason to know identifiable health information by virtue of a treatment relationship with the potential participant.

Clinician -- a physician or service provider who has a treatment relationship with the patient.

Coded Specimens – specimens where (1) Identifiers (see definition below) have been replaced with a number, letter, symbol, or combination of all, and (2) A key to decipher the code exists, enabling the linkage of the code to a specific individual.

Co-investigator – the scientist or scholar who collaborates with the principal investigator in the design and/or conduct of a research project.

Cognitively impaired – having either a psychiatric disorder (e.g., psychosis, neurosis, personality disorder, 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.

Collaborating Entity -- an institution, practice plan, clinic, or individual that is participating in a cooperative research activity with the lead institution. (See the Policy on Collaborating Institutions for more definitions.)

Common Rule (The) – see Federal Policy.

Community Representative: an individual whose primary concerns are those of the population base from which research participants are drawn.

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.

Conflict of Interest -- refers to situations in which the employee and or his/her immediate family has financial or personal interests that may compromise, or have the appearance of compromising, the employee's professional judgment in conducting or reporting research.

Consent Process - the process by which a human participant is informed (understands) what a study entails before voluntarily agreeing (consenting) to participate. The informed consent process begins with recruitment and obtaining a signature on an informed consent document and continues through and beyond the completion of the study.

Continuing Non-compliance - repeated pattern of non-compliance by an individual investigator or research staff member either on a single protocol or multiple protocols.

Coordinating Center – an organization that agrees to accept additional responsibilities for the conduct of a research project. Its employees or agents must maintain an operations center to provide for the scientific oversight and human participant protection for all of the sites involved in the project. Their functions include, but are not necessarily limited to data safety and monitoring, data analysis, protocol development, adverse event reporting and assurance verification.

Covered Entity – a health plan, health care clearinghouse, and health care providers that transmit health information electronically in connection with certain defined HIPAA transactions such as claims or eligibility inquiries. Researchers are not usually considered covered entities unless they are also health care providers and engage in any of the covered electronic transactions. If a researcher is an employee or other workforce member of a covered entity, they may need to comply with HIPAA privacy policies for research for that entity.

Data Safety & Monitoring Board (DSMB) or Committee - a group typically comprised of experts including scientists, physicians, statisticians, bio-ethicists, and others, that meet periodically throughout the course of a research study to monitor: (1) the disease, drug, device, procedure or outcome measures of the research; and (2) methodological issues including design, data management and statistical analysis. These groups are usually external to the research team. Its primary functions are to monitor outcomes to assure the safety of participants and the scientific integrity of the research study. The results of their reviews determine whether or not a study must continue or be closed.

Data and Safety Monitoring Plan - a written description of the principal investigator's (PI) plan to monitor the data and safety of participants enrolled during the course of a study.

Data Use Agreement - the agreement that should be used between the principal investigator (PI) at WSU and the entity to whom the three elements or less of PHI that are considered in a Limited Data Set (see definition below) are being disclosed outside of WSU, but only when the WSU researcher is using only these three elements. A HIPAA Authorization is not required in this case. The HIC template for the Data Use Agreement (DUA) can be found at the HIC website at the HIPAA link (<http://www.hic.wayne.edu/hipaa.html>).

Dead Fetus – a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

Debriefing – giving subjects previously undisclosed information about the research project following completion of their participation in the research. (Note that this usage, which occurs within the behavioral sciences, departs from the standard English, in which debriefing is obtaining rather than imparting information.)

De-Identified Data Set - a data set that has had all 18 elements of PHI **removed prior** to being available to the principal investigator (PI) and his/her research staff members for research purposes.

Delivery – delivery occurs when there has been complete separation of the fetus from the mother by expulsion or extraction or any other means.

Disapproval - the protocol as submitted is such that it cannot be reviewed in its current form and it requires complete revision and resubmission as a new protocol.

Disclosure - the release, transfer, access to, or the divulging of information in any manner outside the entity holding the information. At WSU, when an outside monitor reviews PHI within a medical record or source documents at WSU or one of its affiliate institutions it is **not** considered a disclosure.

Emancipated Minor - there are no conditions under which a child below the age of 16 can be considered emancipated. Under Michigan law, children 16 years of age or older may be emancipated under specific circumstances. See HIC Policy "*Vulnerable Participants: Children as Research Participants.*"

Emergency Use of a Test Article – use of a test article (unapproved drug, device or biologic) on a human participant in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. [21 CFR 56.102(d).

Employee - any person possessing either a full-time or part-time appointment at the University. These include the faculty ranks of professor, associate professor, assistant professor (and all of the foregoing whose appointments contain such terms as "Research," "Adjunct," "Visiting," or "Clinical,") instructor, and lecturer, as well as academic professionals and postdoctoral associates. Employees, students, and other individuals identified as key personnel on grant applications, whether salaried or non salaried, who on behalf of the University are responsible for, or in a position to influence the design, conduct or reporting of the research, or other scholarly activity are also included in this definition.

Ethics – study of the general nature of morals and of the specific moral choices to be made by the individual in his/her relationship with others.

Exempt research - human participant research where the **entire** research project falls within one or more of the six specific regulatory categories (see HIC Policy/Procedure, "Exempt Review") and satisfies all institutional policies and procedures.

Expedited Review - minor changes in previously approved research during the period (of one year or less) for which approval is authorized can be reviewed by the HIC chair, IRB chair, or his/her designee to determine approval.

Family member - includes the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

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 research. Currently, sixteen federal agencies have adopted the Federal Policy. (Also known as the "Common Rule.")

Fetus – the product of conception from implantation until delivery.

Finder's fees – payment (money, goods, or services) to physicians or other professionals for referral or recruitment of a subject to a research project.

For-Cause Audit – an in-depth examination of all components of a research study including, but not limited to all records and documents; observations of processes; and interviews with investigators, research staff members, and participants for the purpose of determining if the rights and welfare of participants are being upheld according to federal regulatory and HIC requirements.

Full Board Review – when revisions are substantive, with increased risk to participants, or there is a significant change to the study design, the revisions must be submitted for review by the full IRB. Full IRB review of a properly submitted Amendment requires review at a regularly scheduled meeting of an IRB that originally reviewed the protocol and a vote by the IRB members.

Genetic Research - research that involves either: (1) The analysis of human chromosomes or DNA from an individual and/or family members for the purpose of deriving information concerning that individual or family about the presence, absence or mutation of genes, DNA markers or inherited characteristics; or (2) Other studies with the intent of collecting and evaluating information about inheritable diseases and/or characteristics within a family.

Health Information - any information whether oral or recorded in any form that is: 1) created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university or health care clearinghouse, and 2) relates to the past, present or future physical or mental health or condition of an individual; provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.

Human Investigation Committee (HIC) - Human Investigation Committee: the name of the institutional review board for Wayne State University and its affiliated health care institutions (i.e., Barbara Ann Karmanos Cancer Institute, Children's Hospital of Michigan, Detroit Receiving Hospital/University Health Center, Sinai-Grace Hospital, Harper University Hospital, Hutzel Women's Hospital, Huron Valley/Sinai Hospital, Rehabilitation Institute of Michigan, John D. Dingell Veterans Administration Medical Center, and the Michigan Orthopedic Surgery Hospital).

HIPAA (Health Insurance Portability and Accountability Act) – a law passed by Congress in 1996 for the protection of the privacy of certain individually identifiable health data (e.g., medical record), referred to as [Protected Health Information (PHI) see definition below].

These regulations (45 CFR 160 & 164 Subparts A and E) were implemented for research on April 14, 2003. (See HIC Policy, "HIPAA Requirements in Research.")

HIC Chair: the individual who directs the proceedings of the HIC in its entirety and who has administrative authority in a wide range of areas related to IRB functions. The HIC Chair is also Chair of the Steering Committee.

Humanitarian Use Device (HUD) – a medical device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect fewer than 4,000 individuals in the United States. An HUD is considered somewhere between research and ordinary clinical practice. These devices do not undergo the same stringent requirements that investigational devices do, yet they may be recognized as the "approved" standard, and in some cases, preferred medical device.

Human Participant (subject) – (1) Under DHHS regulations "human subject" means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. 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. 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. (2) Under FDA regulations "human subject" means an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used. *Note:* Investigators conducting human participant research must satisfy HHS regulations [45 CFR 46], FDA regulations [21 CFR 50 and 56], and VA regulations [38 CFR 16] regarding the protection of human subjects [participants] in research, as applicable. HHS regulations [45 CFR 46.102(f)] and VA regulations [38 CFR 16.102(f)] define a **human subject** as a living individual about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual; or (2) identifiable private information.

Human Subjects – 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. [See "Human Participant (Subject)" definition above.]

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

Interaction - includes communication or interpersonal contact between investigator and participant.

Identifiable private information – includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation 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).

Identifiers – Information that could be associated with a specific research participant [name, address, elements of dates, phone numbers, fax numbers, social security number, medical record number, health insurance number, account numbers, certificate or license numbers, vehicle and serial numbers, device ID and serial numbers, WEB URLs, IP Addresses, biometric identifiers (finger prints, full face photographs or comparable images), any unique identification number, characteristics or codes].

IDE – acronym for “Investigational Device Exemption.” See definition below.

Immediate Family -- an individual’s spouse or domestic partner and dependent children.

IND - acronym for “Investigational New Drug.” See definition below.

Individually Identifiable Health Information - a subset of health information, including demographic information collected from an individual, and: 1) is created or received by a health care provider, health plan, employer, <http://www.hic.wayne.edu/hipaa.html> or health care clearinghouse, and 2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual, and a) identifies the individual, or b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Individually Identifiable Samples - samples obtained by the investigator that have identifiers or a link that permits the determination of the individual participant through the use of a code.

Information Sheet - a document that contains all the required elements of informed consent without a signature line. The act of participation is considered consent.

Informed Consent -- an ongoing process by which a participant or his/her legal representative voluntarily confirms his or her willingness to participate in a particular research project, after having been informed of all aspects of the research that are relevant to the participant’s decision to participate. See HIC Policy, “Informed Consent Options.”

Institutional Conflict of Interest -- consists of two major types: (1) Conflict of Interest involving University equity holdings or a royalty arrangement related to sponsored programs, and (2) Conflict of Interest involving University officials who make decisions with institutional-wide implications, which can include department heads and center and institute directors, in addition to senior management.

Institutionalized – a cognitively impaired/mentally disabled research participant living in a non-voluntary and/or dependent residence in an “institution” (e.g., hospital, group home, etc.) who may not be competent to give informed consent.

Institutional Review Board (IRB): 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 in accordance with federal regulations [45 CFR 46].

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

Interaction: includes communication or interpersonal contact between investigator and participant.

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.

Investigational Device - a medical device that is being studied to evaluate its effectiveness and/or its safety. It is considered investigational if it either: 1) is not approved for marketing in the United States, or 2) the device is approved for marketing but is being evaluated clinically for a new indication/use.

Investigational Device Exemption (IDE) – Is granted by the FDA for clinical trials that use unapproved investigational or medical devices on human subjects. This allows the researcher to use a device that has not undergone the appropriate stages to be a FDA approved device. An IDE is required when the unapproved device poses a significant risk to subjects (21 CFR 812.30).

Investigational New Drug (IND) - application with the FDA has not been released by the FDA for general use, and is not available through regular channels of interstate commerce, but has been granted approval to use for research or humanitarian purposes by the FDA; 2) FDA approved drugs which are used in a non-FDA approved manner under a study protocol (i.e., change in therapeutic indication, dosage, route of administration); and (3) any drug that is deemed “investigational” by the FDA. For all John D. Dingell Veterans Administration Medical Center (JDD VAMC) research, any approved drug that is being studied in a controlled, randomized, or blinded clinical trial is also considered an “investigational drug”. VHA Handbook 1200.5 14(b) & JDD VAMC Appendix A-Procedures for Utilizing Investigational Drugs-1.a(1), (2). The term investigational drug and investigational new drug are deemed to be synonymous for purposes of this part” [see 21 CFR 312.3(b)].

Investigator - anyone (whether professional or student) involved in the conduct of research.

Key Personnel – all individuals responsible for the design and conduct of the study. This includes those individuals responsible for the recruitment and consent of potential study

participants.

Lead Institution -- the institution that is awarded the grant/contract or is leading the research project if unfunded.

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 (45 CFR 46.102). In the case of children, this would be a parent or legal guardian. For adults, a legally authorized representative would have durable power of attorney for health care for the subject or some other court order authorizing him/her to be the legal representative.

Life-Threatening/(Fatal) Adverse Reaction/Unexpected Event (AR/UE) – this includes both life-threatening and severely debilitating conditions, according to 21 CFR 56.102(d): (1) Life-threatening means a high likelihood of death unless the course of the patient/participant's condition is interrupted. It includes diseases or conditions with potentially fatal outcomes, where the end point of trial analysis is survival. Immediacy of death is not required. The participants must be in a life-threatening situation requiring intervention before IRB review at a convened meeting is feasible. (2) Severely debilitating means diseases or conditions that cause major irreversible morbidity such as blindness, loss of an extremity, loss of hearing, paralysis or stroke.

Limited Data Set - when a researcher at WSU and its affiliates is using only the elements of Protected Health Information (PHI) that include: 1) the address greater than street address, 2) elements of dates, and 3) the unique identifying number, characteristic or code.

Management Plan -- a plan developed by the FCOI Committee that places requirements on a relationship to reduce or eliminate factors that may compromise objectivity in the conduct of the research

Medical Device -- any health care product that does not achieve its primary intended purpose by chemical action or by being metabolized (e.g., surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, stents, intraocular lenses, orthopedic pins, diagnostic aids such as reagents and test kits for *in vitro* diagnosis of disease and other medical conditions).

Minimal Risk – the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Minor Modifications - a change that would not materially affect an assessment of the risks and benefits of the study, does not substantially change the specific aims or the design of the study, and all added procedures meet the applicability criteria and fall into one or more categories defined in the *Expedited Review* section of the HIC Policy/Procedure.

Moderate Adverse Reaction/Unexpected Event (AR/UE) – an event that requires medical evaluation (such as additional laboratory testing) and/or medical treatment.

Neonate (newborn) - refers to the human child from birth to four weeks of life.

Non-Compliance- failure to comply with regulations, requirements, or determinations of the IRB and federal regulatory agencies. See HIC Policy, "Reporting of Unanticipated Problems, Terminations, Suspensions, and Serious & Continuing Non-Compliance."

Non-Institutionalized – relates to a cognitively impaired/mentally disabled individual residing as an inpatient or outpatient who is free-living, but may not be competent to give informed consent.

Non-Serious or Minor Adverse Reaction – an event that is expected (is already stated in the consent form), but is more frequent, longer lasting, and/or more intense than was described.

Non-Significant Risk Device (NSR) - a device that does not meet one or more of the criteria for a significant risk device is considered a non-significant risk device. In other words, it is not an implant; not used to support or sustain human life; not of substantial importance in diagnosing, curing, mitigating or treating disease; is not significantly involved in preventing impairment of human health; or does not present a potential risk or serious risk to the health, safety or welfare of a subject [21 CFR 812.2(b)].

Nonviable Neonate – refers to a neonate after delivery that, although living, is not viable, i.e., does not have the ability to survive after delivery.

Off-Site AR/UE - an event that occurs/is observed at an external site and is reported to a WSU principal investigator (PI) by external sponsors or the PI of multi-center studies.

Office for Human Research Protection (OHRP) – an 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 46) governing research involving human subjects.

On-site AR/UE - an event that occurs at Wayne State University (WSU) and/or at any of its affiliated institutions or those sites for which WSU is acting as the Coordinating Center and is under the jurisdiction of this IRB.

Oral Assent – an affirmative verbal agreement by an individual not competent to give legally valid informed consent to participate in a research study.

Oral Consent –process of obtaining consent without the use of a written document.

Parent – a child's biological or adoptive parent.

Parental Permission – the agreement of parent(s) or guardian(s) to the participation of their child or ward in research.

Phase 1 Study - includes the initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer participants (subjects). These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. "Phase 1 studies also include studies of drug metabolism, structure-activity relationships, and mechanism of action in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes." [21 CFR 312.21 (a) (2)] Noted as "Clinical Pharmacology Trial" according to JDD VAMC Appendix A, 1.g. (1) A-1.

Phase 2 Study - includes the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug. Phase 2 studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects (participants)" [21 CFR 312.21(b)] Noted as "Clinical Pharmacology" Trial according to JDD VAMC Appendix A, 1.g. (2) A-2.

Phase 3 Study - expanded controlled and uncontrolled clinical trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather the additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 studies usually include from several hundred to several thousand subjects (participants)" [21 CFR 312.21(c)] Noted as "Extensive Clinical Trial" according to JDD VAMC Appendix A, 1.g. (3) A-2.

PHI – acronym for "Protected Health Information." See definition below.

Placenta - is the vascular structure in the uterus of the mother that provides oxygen and nutrients for, and transfers wastes from, the developing fetus.

Planned Emergency Research - research that involves participants (subjects) who, because of their condition (e.g., unconsciousness) are in a life-threatening situation that makes intervention necessary, are unable to give informed consent, and to be effective, the intervention must be administered before informed consent from the subject's legally authorized representative is reasonably possible.

Pregnancy – encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of pregnancy test are negative or until delivery.

Principal Investigator: (1) The Office of Human Research Protections (OHRP) Guidebook defines Principal Investigator as "the scientist or scholar with primary responsibility for the design and conduct of a research project." (2) The Veterans Administration Handbook (VAH) 1200.53 (t) defines a Principal Investigator as "an individual who conducts a research

investigation (i.e., under whose immediate direction research is conducted) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.”

Principal Investigator (PI) at Lead Institution – the *one* individual who is responsible for the conduct of the research protocol and the research project at the Lead Institution. A research protocol or project may have multiple collaborating institutional relationships but there is only *one* principal investigator.

Prisoner – any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute; as well as 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.

Prisoner Subcommittee – a subcommittee of the HIC Steering Committee approved by the HIC Chair to review all protocols in which principal investigators propose to enroll prisoners.

Privacy Board - a board that is established to review and approve requests for waivers or alterations of authorization regarding use or disclosure of Private Health Information (PHI). In the case of WSU and its affiliate institutions, including the John D. Dingell VA Medical Center (JDD VAMC), the HIC serves as the privacy board to review the effect of a research protocol on an individual's privacy rights and related interests.

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 participant 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 participants.

Prospective Study - a study in which the collection of specimens will occur “in the future”. In other words, the biological specimen is not “on the shelf” when approval for the research under review is requested. This may refer to: (1) Specimens that will be obtained specifically for research purposes after the research protocol has been approved by the IRB wherein the participant is asked to undergo a procedure to obtain a specimen for research purposes, or (2) Specimens to be collected from discarded clinical samples that will be obtained after the research is approved by the IRB.

Protected Health Information (PHI) – includes personal and/or identifiable information about a research participant that may be contained in medical records including but not limited to name, address, telephone numbers, fax numbers, social security number, medical record number, health insurance number, certificate/license numbers, vehicle and serial numbers, biometric identifiers (voice and fingerprints), full face photographs and any unique identifying numbers or characteristics or codes.

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.

Research – (1) Under DHHS regulations, “research” means a systematic investigation, including development, testing and evaluation, designed to develop or contribute to generalizable knowledge. (2) Under FDA regulations research means 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 FDA under section 505(i) or 520(g) of the Food, Drugs, and Cosmetics Act, or need not meet the requirements for prior submission to the FDA under these sections of the Food, Drug, and Cosmetics Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. For research involving drugs, an experiment is any use of a drug, except for the use of a marketed drug in the course of medical practice, and is defined as a systematic investigation designed to develop or contribute to generalizable knowledge.

Note: If the research activity does not qualify under any of the above circumstances, then the activity would not need to be submitted and reviewed by the HIC. If a PI has questions about whether or not a research activity requires IRB review, consultation with the Human Investigation Committee Office (HIC) is strongly recommended.

Retrospective Study -- a study that utilizes existing specimens that have already been collected when the request for review and approval is made. This may refer to: (1) tissue collected for clinical indications and then stored (i.e., pathology specimens, leftover serum); or (2) a secondary use of tissue collected previously for another research protocol (material in a tissue bank).

Risk – the probability of harm, injury, or loss (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. Physical risks may arise from the use of test agents such as chemicals or therapeutic drugs, devices, physical agents (including radiation), and clinical procedures. Psychological risks may arise from the utilization of behavioral questionnaires or surveys, interview interactions, the collection of sensitive data, or the emotional stress of study participation. Social risks may arise from actual or potential breaches of confidentiality or anonymity such as harm to interpersonal relationships, damage to reputation or social standing, or exposure to legal sanctions. Economic risks may affect an individual's financial status, employability or insurability.

Scientist: an individual whose primary concerns are in scientific areas and whose expertise is relevant to one or more areas of research that are reviewed by the HIC

Serious Adverse Reaction/Unexpected Event (AR/UE) - an event that requires or prolongs hospitalization, produces a disability, or results in a congenital anomaly/birth defect or is judged to be serious by the PI.

Serious Non-Compliance - failure to comply with regulations, requirements, or

determinations of the IRB and federal regulatory agencies. See HIC Policy, "Reporting of Unanticipated Problems, Terminations, Suspensions, and Serious & Continuing Non-Compliance."

Significant Financial Interest - anything of monetary value, including but not limited to, salary or other payment for services (e.g., consulting fees or honoraria), equity interests (e.g., stocks, stock options or other ownership interests) and intellectual property rights (e.g., patents, copyrights and royalties from such rights).

Significant Risk Device (SR) - a device that may present a potential for serious risk to the health, safety or welfare of a participant and is (1) intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject is considered a significant risk device [21 CFR 812.3(m)].

Site Principal Investigator – the one individual at the collaborating entity who is responsible for the conduct of the research protocol and the research project at that site.

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.

Specific Minor Revisions - this outcome requires that minor changes (but no new information is required by the full IRB to determine the risk/benefit ratio) be made to the protocol before approval to begin can be granted. The minor changes must be submitted to the IRB within 60 days of the initial outcome.

Student/Trainee – any individual who is enrolled in a graduate or undergraduate program at WSU and those individuals who are in training programs conducted by WSU.

Substantive Modifications (*changes that are more than minor*) - any revisions to a study that involve increased risk to participants or significantly affect the design of the study must be reviewed by the full IRB. For example, revisions to the recruitment plan, adding or revising eligibility criteria, and newly identified side effects or adverse events related to the study drug.

Suspension – a suspension occurs when the Assistant Vice President for Research (AVPR), HIC Chair, IRB Committee or IRB Chair places a temporary hold on research that had previously been approved so that no new participants can be accrued, no research interventions may occur (unless necessary for the safety and well-being of the enrolled participants) and no follow-up can be conducted unless it is in the best interest of the participant and approved by the IRB.

Tabled (Substantive Revisions) - a number of significant questions and concerns regarding the risk/benefit ratio require resolution before the research protocol can be approved by the IRB.

Terminally III – (1) Imminent death – reasonably expected survival is greater or less than one

week; (2) shortened life expectancy – reasonably expected survival is greater than one week but greater or less than six months due to a currently recognized illness.

Termination of a previously approved protocol – termination of a previously approved protocol occurs when the IRB withdraws approval or stops all research activity permanently. No new participants may be enrolled and no additional research interventions can occur. However, future follow-up may be conducted with the approval of the IRB to monitor the well-being of and any potential risk to participants enrolled prior to termination.

Test article - any drug, biological product, or medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation under the Federal Food, Drug and Cosmetic Act (21 CFR 50.3(j),) or under sections 351 or 354-360F of the Public Health Service Act (VHA 1200,5 3,y)

Treatment Use (Compassionate) of Investigational Medical Device - under an existing Investigational Device Exemption (IDE) the FDA may allow treatment with a medical device of a small number of seriously ill patients who have no other acceptable alternatives. The FDA requires the sponsor/investigator to provide a supplement to an existing IDE justifying the “compassionate use.”

Treatment Use of an Investigational Drug or Biologic - use of an investigational drug or biologic with a person or group of persons with a serious or debilitating condition where there are no other treatment options available.

Unexpected Event (UE) - an unanticipated problem involving risks to participant or others. Any event or information that: (1) was unforeseen and (2) indicates that the research procedure caused harm to participants or others or indicates that the participants or others are at increased risk of harm. Unexpected Events may occur in non-clinical (behavioral or social science) as well as clinical research studies. Unexpected Events will never be listed in the original informed consent document.

Viable – as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

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.

Waiver of Consent for Other Reasons – consent may be waived by the IRB if the following four conditions are met: 1) the risk to the subject is not more than minimal 2) the waiver will not adversely affect the rights and welfare of the research participants 3) the research could not practicably be carried out without the waiver, and 4) the subjects will be provided with additional pertinent information after participation when appropriate.

Waiver of Consent in Emergency Situations – in acute medical emergency research, situations may arise in which the patient cannot give consent, nor can his/her legally

authorized representative be contacted in time to consent to the investigational therapy. Waiver of written informed consent must be pre-approved by the HIC prior to enrollment of patients under these conditions.

Witness – a person, who is independent of the research team and cannot be unfairly influenced by people involved with the research, who does not have a coercive relationship with the participant, who attends the informed consent process when the participant or the participant's legally authorized representative is illiterate or legally blind. A witness is required when using a translated consent.

Written Assent – a signed document used to record the agreement by an individual not competent to give legally valid consent (e.g., a child or cognitively impaired person) to take part in a research study.

Written Consent – a signed document used to record the agreement by an individual competent to give legally valid consent to take part in a research study.