

Allegation of noncompliance – An unproven assertion of noncompliance.

Assent: A child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent (*45 CFR 46.402(b)*).

Administrative Hold: A voluntary action by an investigator to temporarily or permanently stop some or all approved research activities in response to a request by the convened IRB or IRB designee to take such action. Administrative holds are not suspensions or terminations.

Adverse event - Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice). Adverse events encompass both physical and psychological harms. (*OHRP Guidance Document, “Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events”*)

Amendment: Any change to a study from what was previously approved during the period for which approval was given.

Clinical Investigation –(as defined by FDA regulation)“any experiment that involves a test article and one or more human subjects and that and that is one of the following: [*21 CFR 50.3 (c)*][*21CFR 56.3(c)*]

- i. subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the(FDA) act; ii. not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit;
- iii. the term does not include experiments that are subject to the provisions of 21 CFR 50.3(g).

Conflict of Interest (COI) - Instances when there is a convergence between an individual’s personal financial, relational, or other interests and his/her professional obligations to the University of Missouri such that an independent observer might reasonably determine that the individual’s professional actions or decisions are adversely affected, distorted or otherwise compromised by the individual’s personal interests.

SECTION 330.015 of the Collected Rules and Regulations of the University of Missouri requires that a University employee shall make a full disclosure in writing of her or his present or proposed outside financial interest to the

appropriate University official for filing in a registry located for public scrutiny in the following circumstances:

- When a University employee engages in any outside matters of financial interest incompatible with the impartial, objective, and effective performance of their duties; such as, when it is proposed that the University enter into (a) contracts for the sale of goods or services, or (b) research contracts, or (c) other contracts, including those for technological transfer, with private firms or corporations in which a University employee knows he or she has a direct or indirect financial interest.
- When the financial interest of the University employee in the private firm or corporation is such that it could influence the decision-making process of the private firm or corporation and the employee could also influence the decisionmaking process of the University in entering into or performing the contract. • Realize personal gain in any form which would influence improperly the conduct of their University duties.
- When there is a change in the University employee's financial interest during the course of such contracts.
- When an employee enters into a business activity which overlaps with the University's teaching, research, or service missions; such as, when an employee of the University teaches either credit or non-credit courses not connected with the University.
- When a business interest for which the employee consults and the entity conducts business with the University, is in competition with the University, or competes with the work of the University.

(see <http://research.missouri.edu/complia/coi.htm> for the complete policy and disclosure form)

Children: DHHS: “children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.”(45 CFR 46.402(a))

FDA: “children means persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.” (21 CFR 50.3(o)).

Compensation – Any payment to a study participant which may be in the form of cash, credit, voucher, or gift. Payment to research participants in studies is not considered a benefit; rather, it should be considered compensation for time and inconvenience associated with participation in research activities, or recruitment. Payments may be in the form of cash or non-cash.

Confidentiality: the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.

Continuing noncompliance - the systematic and habitual disregard of restrictions, procedures, stipulations, or decisions of the IRB.

Cooperative research is defined as research conducted in cooperation with and at a performance site of an institution or facility that is not affiliated with UMC or that does not fall under the UMC IRB's authority. An off-site institution or facility may be domestic or international and may or may not have its own IRB.

Dead fetus: An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord. (45 CFR 46.202(a)).

Decisionally impaired: Individuals who have a diminished capacity for judgment and reasoning due to a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals, who may be considered decisionally impaired, with limited decision-making ability, may include: Individuals under the influence of or dependent on drugs or alcohol, traumatized individuals, individuals suffering from degenerative diseases affecting the brain, terminally ill patients, individuals with severely disabling physical handicaps, individuals who have lost cognitive ability due to trauma, anesthetics, analgesics, or extreme pain, such as in an emergency room setting or preparatory to surgery

Emergency Use: The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB approval. (21 CFR 56.102(d))

Expiration of approval: If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, such research is said to have expired approval.

Fetus: The product of conception from the time of implantation until delivery. (45 CFR 46.202 (c)).

Financial Interests Related to the Research – Financial interest in or from the sponsor of the research or an entity or financial interest in or from a product or service being tested in research.

Financial (Direct) Interest – Any relationship entered by any member of the study team, other than employment by the University of Missouri (or the primary employment of non-MU collaborators), which could result in financial gain for the individual or his/her

immediate family (ie. spouse and dependent children) Financial interest includes but is not limited to consulting, speaking or other fees; honoraria; gifts; patent, trademark, copyright or licensing revenues, and equity interests or stock options irregardless of amount.

Finding of noncompliance – A proven assertion of noncompliance.

Generalizable Knowledge: Investigations *designed to develop or contribute to generalizable knowledge* are those designed to draw general conclusions, inform policy, or generalize findings beyond a single individual or an internal program (e.g., publications or presentations.) However, research results do not have to be published or presented to qualify the experiment or data gathering as research. The intent to contribute to "generalizable (scholarly) knowledge" makes an experiment or data collection research, regardless of publication.

Guardian: An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.(45 CFR 46.402(e)).

Human Subject (as defined by DHHS regulation)– “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 and manipulations of the participant or the participant’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. 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 subjects [45 CFR 46.102(f)]

Human Subject (as defined by FDA regulation) “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 human or a patient” [21 CFR 56.102(e) – for FDA regulated drug, food or biologic research], *or*

“A human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or who participates as a control. A subject may be in normal health or may have a medical condition or disease.” [21 CFR 812.3(p) – for FDA regulated device research]

IRB Designee: The IRB Chair, IRB Vice-Chair, IRB Manager, Intuitional Official, or a person designated to temporarily assume the role of one of those persons.

Incapacity: An individual'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.

Informed Consent: An ongoing process whereby a subject voluntarily agrees, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. The subject must not feel coerced or perceive undue influence that results in the agreement to participate. 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 from liability for negligence.

Interaction: includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f)).

Intervention: includes both physical procedures by which data are gathered and manipulations of the participant or the participant's environment that are performed for research purposes. *Interaction* includes communication or interpersonal contact between investigator and subject. (45 CFR 46.102(f)).

Interpreter: someone who mediates between speakers of different languages.

Key Personnel – All persons who will be obtaining consent, acquiring data, performing data analysis, generating a final report, or other duties related to the study must be listed as study personnel and have the appropriate training that is up-to-date.

Life Threatening: For the purposes of 56.102(d) includes the scope of both life-threatening and severely debilitating, as defined below:

- Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
- Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Legally Authorized Representative (LAR): 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(c)).
(For research taking place in Missouri, see Missouri Statute Chapter 431, Section 431.064)

Minimal risk: 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. (45 CFR 46.102(i) and 21 CFR 50.3(k)).

Minimal risk for research involving prisoners: The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. 45 CFR 46.303(d) and 21 CFR 50.3(o)).

Noncompliance: failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determination of the IRB with respect to conduct of the research as approved by the IRB. For VA studies, this includes failure to follow the requirements of VHA Handbook 1200.5.

Non-financial (Indirect) Interest - Private interests include unpaid leadership positions, membership on the board of directors, companies, clubs, societies and organizations such as trade unions and voluntary organizations, which members of the public might reasonably think could influence the decision-making process.

Non-English Speaking Subject: A person whose primary language is other than English. This includes persons who have a limited ability to read English and/or understand spoken English.

Non-scientist: Nurses, pharmacists and other biomedical health professionals are not regarded as having "primary concerns in the non-scientific area." Lawyers, clergy, ethicists, and social workers are examples of persons whose primary concerns would be in non-scientific areas. Members who have training in both scientific and non-scientific disciplines, such as a J.D., R.N. will not be appointed to satisfy the non-scientist requirement. (FDA Information Sheet, "IRB Membership")

Non-significant risk device: A non-significant risk device is one that does not meet the definition for a significant risk device. Examples of non-significant risk devices include low power lasers for treatment of pain, daily wear contact lenses and associated lens care products not intended for use directly in the eye, Magnetic Resonance Imaging (MRI) devices within FDA specified parameters, Ob/Gyn diagnostic ultrasound within FDA approved parameters, wound dressings (FDA Information Sheet, "Medical Devices")

Off-site research designates research conducted at performance sites that are not owned or operated by UMC, at non-UMC sites that are geographically separate from UMC, or at sites that do not fall under the UMC IRB's authority.

Protocol: The plan for a course of medical treatment or for a scientific experiment. A protocol should include the following components (when applicable): the study title, the purpose of the study, the sponsor, results of previous related research, participant inclusion/exclusion criteria, Justification for use of any special/vulnerable participant population, study design, description of the procedures to be performed, provisions for managing adverse reactions, the circumstances surrounding consent procedure, the procedures for documentation of informed consent including any procedures for obtaining assent from minors, using witnesses, translators and document storage, compensation to participants for their participation, any compensation for injured research participants, provisions for protection of participant's privacy, extra costs to participants for their participation in the study, and extra costs to third party payers because of an individual's participation (*FDA Information Sheets, A self-evaluation checklist for IRB's*)

Protocol violation - Any deviation from the protocol that is not approved by the IRB prior to its initiation or implementation.

Parent: Minor's biological or adoptive parent.(45 CFR 46.402(d)).

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, 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. (45 CFR 46.303(c)).

Privacy – Freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.

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. 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 subjects [45 CFR 46.102(f)]

Protected Health Information (PHI) : *Protected health information* means individually identifiable health information:

(1) Except as provided in paragraph (2) of this definition, that is:

- (i) Transmitted by electronic media;
- (ii) Maintained in electronic media; or
- (iii) Transmitted or maintained in any other form or medium.

(2) Protected health information excludes individually identifiable health information in:

- (i) Education records covered by the Family Educational Rights and Privacy Act, as amended, 20 U.S.C. 1232g;
- (ii) Records described at 20 U.S.C. 1232g(a)(4)(B)(iv); and
- (iii) Employment records held by a covered entity in its role as employer. (45 CFR Part 160.103)

Recruitment: To solicit, communicate, question a potential subject with the intention of enrolling them into a research project under the jurisdiction of the University of Missouri-Columbia.

Related – the causality of the problem has been determined to be definitely, probably or possibly attributable to the research procedures or it is more likely than not to affect the rights and welfare of current participants.

Research – (as defined by DHHS regulation) “a systematic investigation designed to develop or contribute to generalizable knowledge” [45 CFR 46.102(d)], or Clinical Investigation (as defined by FDA regulation) “any experiment that involves a test article and one or more human subjects and that is one of the following: [21 CFR 50.3 (c)][21CFR 56.3(c)]

- i. subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the(FDA) act; ii. not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit;
- iii. the term does not include experiments that are subject to the provisions of 21 CFR 50.3(g).

Systematic Investigation: A "*systematic investigation*" is an activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

Generalizable Knowledge: Investigations *designed to develop or contribute to generalizable knowledge* are those designed to draw general conclusions, inform policy, or generalize findings beyond a single individual or an internal program (e.g., publications or presentations.) However, research results do not have to be published or presented to qualify the experiment or data gathering as research. The intent to contribute to "generalizable (scholarly) knowledge" makes an experiment or data collection research, regardless of publication.

Research (scientific) misconduct- fabrication, falsification, plagiarism or other practices that seriously deviate from those that are commonly accepted within the academic community for proposing, performing, or reviewing research, or reporting research results. Misconduct does not include honest error or honest differences in interpretations or judgments of data.

Collected Rules -420.010 Research Dishonesty

<http://www.umssystem.edu/ums/departments/gc/rules/research/420/010.shtml>

Risks – the occurrence of harm or probability that harm might occur. The harm may be physical, psychological, financial, social, economic, or legal.

Serious noncompliance - All noncompliance substantially affecting participants' rights or welfare, or impacting upon the risks or benefits is serious noncompliance.

Significant risk device: An investigational device that:

- (1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a participant;
- (2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a participant;
- (3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a participant; or
- (4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a participant. (21 CFR 812.3(m)).

Sponsor: means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator) and the employees are considered to be investigators. (21 CFR 56.102 (j))

Sponsor-investigator: means an individual who both initiates and actually conducts, alone or with others a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator. (21 CFR 56.102 (k))

Suspension: A directive of the convened IRB or IRB designee either to temporarily or permanently stop some or all previously approved research activities short of stopping

permanently some previously approved research activities. Suspended protocols remain open and require continuing review.

Systematic Investigation: A "systematic investigation" is an activity that involves a prospective plan that incorporates data collection, either quantitative or qualitative, and data analysis to answer a question.

Termination: A directive of the convened IRB or IRB designee to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

Test article: means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act. [21 CFR 50.3(j)] (21 CFR 56.102 (l)).

Translation: written communication in a second language having the same meaning as the written communication in a first language.

Unanticipated adverse device effect – any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (include supplementary materials), or any other unanticipated serious problem associated with a device that related to the rights, safety, or welfare of subjects.

Unanticipated problem involving risk to participant or others - any incident, experience, or outcome that meets **all** of the following criteria:

- (1) unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- (2) related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- (3) suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

(OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events).

VA Investigator – An individual who receives a full or part-time VA salary or any individual who is appointed on a Without Compensation (WOC) basis and is approved by the Research and Development (R&D) Committee to access VA space, equipment, records, or study participants (either patients and/or employees) for research purposes. In the case of an investigator with a dual appointment at both the Harry S Truman Memorial Veterans Hospital (HSTMVH) and MU, the investigator will not be defined as a VA investigator under the following circumstances: (a) if the research activities involve exclusively MU time and resources and do not involve any VA time or resources, and (b) if a disclaimer of VA involvement is signed by the investigator and submitted to the VA Research Office.

VA Participants – Participants recruited at the VA through their affiliation with the VA either as inpatients, VA clinical outpatients or VA medical records.

VA Research- Any research conducted by a VA investigator while on VA employment time, any research conducted by a VA investigator or outside investigator utilizing VA space (offices, labs, etc.), or any research conducted utilizing VA participants.

VA Space/Equipment– Office space, laboratory space or equipment located within the boundaries of the VA Hospital and/or Clinics.

Ward: a child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law.

Witness: Impartial 3rd party to observe the consent process whose role it is to ensure that the information presented orally to the participant is the same as that presented in the written document, to ensure no coercion has occurred and/or ensure that in the event the participant cannot personally sign the consent, they witnessed affirmation on the part of the participant.

Research Involving a Human Being as an Experimental Subject is defined as an activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction [32 CFR 219.102(f), reference (c)]. Examples include, but are not limited to, a physical procedure, a drug, a manipulation of the subject or subject's environment, the withholding of an intervention that would have been undertaken if not for the research purpose.

The term *DoD Components* refers collectively to the organizational entities within the DoD that are subject to the human subjects protections laid out in Department of Defense Directive 3216.02. These entities include the Office of the Secretary of Defense, the Military Departments, the Chairman of the Joint Chiefs of Staff, the Combatant

Commands, the Office of the Inspector General of the Department of Defense, the Defense Agencies, the DoD Field Activities, and all other organizational entities within the DoD.

Support of a study generally means the provision of funding, personnel, facilities, and all other resources. Under this definition, studies that may be wholly funded internally or by a non-DoD component, such as an agency within the Department of Health and Human Services, but focus, for example, on a health concern prevalent in military populations may still fall under DoD purview. Such studies may, for example, require the commitment of military personnel as subjects or the use of DoD data resources.

A *DoD Addendum* to the institution's existing FWA is one of many methods that can be used to inform institutions (Institutional Officials and IRB chairs) of DoD research requirements that differ from the OHRP-approved FWA. These may include designation of the relied-upon IRB(s), an outline of requirements specific to a given DoD Component. The DoD Addendum is effective as long as the FWA is in force.

Research Monitor refers to a physician, dentist, psychologist, nurse, or other healthcare provider designated to oversee a specific protocol that involves more than minimal risk, especially issues of individual subject/patient management and safety. The research monitor functions independently of the research team and shall possess sufficient educational and professional experience to serve as the subject/patient advocate.

Prisoner of War refers to any person captured, detained, held, or otherwise under the control of DoD personnel (military and civilian, or contractor employee). Such persons include: Enemy Prisoners, Civilian Internees, Retained Persons, and Lawful and Unlawful Enemy Combatants. This definition excludes DoD personnel being held for law enforcement purposes.