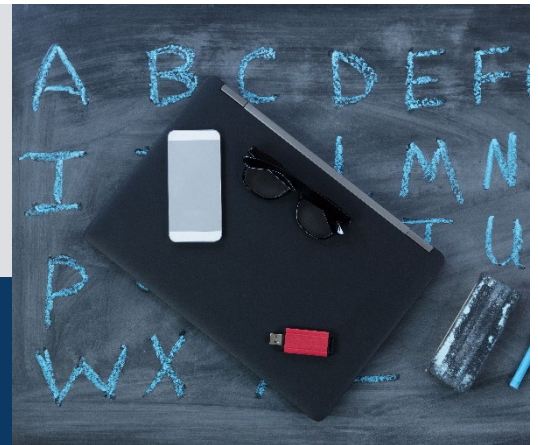


Dictionary of Institutional Review Board (IRB) and Human Research Terms

A guide to IRB terms – some are specific to IRB/human research, and some have different meanings in this arena.



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A

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. Adverse events encompass both physical and psychological harms.

Annual Administrative Review (AAR): the annual review for Expedited protocols that were approved under the 2019 Common Rule and are not FDA-regulated.

Assent: the affirmative agreement of a child or an individual with impaired consent capacity to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Authorization: a document signed by the subject that gives the researcher permission to use/disclose PHI collected during the research study for defined purposes.

Authorization Agreement (also called a Reliance Agreement): identifies and describes the respective authorities, roles, responsibilities, and methods of communication between an institution/organization providing the ethical review of research and a participating site relying on the institution/organization.

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B

Business Associate Agreement: a contract where a person or entity performs certain functions or activities that involve the use and/or disclosure of PHI.

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C

Central IRB (CIRB)/Single IRB (sIRB): the selected IRB of record that conducts the ethical review of research for all participating sites of a multi-site study.

Child or Children (Kentucky): all individuals under 18 years of age unless the individual(s) is legally emancipated. (See section Emancipated Individuals for details of Kentucky state law.) Individuals under 18 years of age who are not emancipated meet the federal definition for “child” [e.g., U.S. Department of Health and Human Services (HHS), Food and Drug Administration (FDA), and U.S. Department of Education].

Clinical investigation (FDA): involves use of a test article (i.e., drug, device, food substance, or biologic), one or more human subjects, meets requirements for prior submission to the FDA (involves drugs or medical devices other than the use of FDA approved drugs or medical devices in the course of medical practice), or results are intended to be part of an application for research or a marketing permit.

Clinical Trial (National Cancer Institute (NCI) and the Markey Cancer Center): a type of research study that tests how well new medical approaches work in people. These studies test new methods of screening prevention, diagnosis, or treatment of a disease. Examples include therapeutic and prevention intervention or non-intervention trials (e.g., patient records, epidemiologic/observation, screening, early detection diagnostic studies).

The Common Rule: the set of federal regulations from HHS which governs IRB practices, review types, and the consent process in human subject research. Widely adopted by federal agencies, an updated version went into effect in January 2019. Here at UK, we refer to the prior version as the pre-2019 rule and the current version as the 2019 rule.

Compassionate Use (single patient or small group): allows access to investigational devices for treatment of a serious disease or condition where no alternative exists, and the patient(s) do not meet the criteria for participation in existing clinical investigations.

Confidentiality: concerns data protections and safeguards.

Conflict of Interest: involves any situation in which an IRB member or consultant has any significant personal or financial interest in the proposed research or clinical investigation. Examples of a conflicting interest are if the IRB member or consultant is any of the following:

- Principal investigator (PI);
- Co-investigator;
- Study personnel receiving funding from the study, as listed in the study budget;
- A supervisory role over the PI of the study (e.g., graduate advisor);
- Family member of PI.

Continuation Review (CR): the annual review for:

- Full Review protocols (reviewed by the convened board)
- Expedited protocols that were approved under the 2019 Common Rule and are FDA-regulated
- Expedited protocols that were approved under the pre-2019 Common Rule

Continuing noncompliance: persistent failure to adhere to the laws, regulations, or policies governing human research.

Controverted Issue: issues that cause controversy and dispute among IRB members during a convened meeting. Controverted issues and their resolution must be documented in minutes of the convened meeting.

Convened Review: A type of IRB review conducted by the full IRB committee at a convened meeting.

Cover letter: For IRB purposes, “Cover Letter” refers to a type of consent document. These are concise presentations of the required elements of consent, and often used at the beginning of research surveys.

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Decedent Research: research where PHI is collected from a subject(s) that is deceased prior to the initiation of the study.

De-identified Information: health information that cannot be linked to an individual.

Detainee: any person captured, detained, held or otherwise under the control of DoD personnel (military, civilian, or contractor employee). It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power.

DoD: Department of Defense

DoD Addendum to the institution’s existing FWA: one of several methods that can be used to inform institutions (Institutional Officials and IRB chairs) of DoD research requirements that differ from the OHRP-approved FWA. The DoD Addendum may include designation of the relied-upon IRB(s) and/or an

outline of requirements specific to a given DoD Component. The DoD Addendum is effective if the FWA is in force.

DoD Components: 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.

DoD Personnel: includes DoD civilian employees and members of the military services, unit officers, and noncommissioned officers (NCOs).

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E

Emergency Use: the use of a test article (e.g., investigational drug, biologic, or device) in a human subject 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.

Exceptions or deviations: changes that impact individual subjects and do not change the overall protocol. Investigators may not implement these changes without prior IRB review and approval except where necessary to eliminate apparent hazards to the subject(s).

Exempt Review: A type of IRB review for research activities in which the only involvement of human subjects is in one or more of the Exempt Research Categories described in 45CFR 46.104. Exempt research is generally reviewed by one IRB member.

Expanded Access (sometimes called Compassionate Use): a mechanism to facilitate availability of investigational drugs (as early in the drug development process as possible) for patients with serious or immediately life-threatening diseases or conditions for which there are no satisfactory alternative treatments.

Expedited Review: A type of IRB review for certain kinds of research involving no more than minimal risk, and for minor changes in approved research. Expedited categories are described in 45CFR46.110. Expedited research is generally reviewed by one IRB member.

External Event/Problem: one that occurs with research subjects enrolled in multi-center research projects that do not fall under the purview of the UK IRB.

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F

FDA: Food and Drug Administration

Federalwide Assurance (FWA): a formal, written, binding attestation in which an institution ensures to the U.S. Department of Health and Human Services (HHS) that it will comply with applicable regulations governing the protection of human subjects.

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G

Guardian (Kentucky): an individual who may serve as a LAR as defined above and meet the federal definitions for a guardian.

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H

HHS: Department of Health and Human Services; first codified the Common Rule

Honest Broker: - an individual or system who collects and provides de-identified information/samples to a recipient secondary researcher. The honest broker should not be involved with the recipient's study. For Protected Health Information, the honest broker should de-identify data or samples according to [HIPAA safe-harbor standards](#) before sending it to the researcher.

Human subject (FDA): an individual who is or becomes a participant in research either as a recipient of a test article or as a control or as an individual on whose specimen a device is used. A subject may be either a healthy individual or a patient [21 CFR 56.102(e)] (Drug, Food, Biologic).

Human subject (FDA for medical devices): a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease [21 CFR 812.3(p)] (Medical Devices). This definition includes the use of tissue specimens even if they are unidentified.

Human Subject (HHS): a living individual about whom an investigator (whether professional or student) conducting research: (1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Human Subject (UK): typically means only “living individuals”; however, at UK, research involving fetal tissue requires IRB review. Other exceptions involving collection of human specimens in FDA regulated device research may apply.

Humanitarian Device Exemption (HDE): a Food and Drug Administration (FDA) marketing application that is similar to a premarket approval application but is exempt from the effectiveness requirements of the medical device law, provided the device meets safety conditions and will not expose patients to significant or unreasonable risk. An HDE approval is based on safety and probable benefit.

Humanitarian Use Device: a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year.

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Immediately Life-threatening Disease (FDA): a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

Institutional Official (IO): the signatory on the FWA filed with the Office for Human Research Protections (OHRP). OHRP requires the IO to be a high-level official who has the authority to represent the institution named in the FWA. The VPR serves as the IO for UK and is responsible for signing IAAs and Individual Investigator Agreements (IIAs) on behalf of the institution.

Interaction (HHS): includes communication or interpersonal contact between investigator and subject.

Internal Event/Problem: one that occurs with research subjects enrolled in a project approved by the UK IRB and directed by an investigator employed by the University or one whose project is under the purview of the UK IRB.

Intervention (HHS): includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Investigational Device: a medical device which is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. The device is still in the developmental stage and is not considered to be in commercial distribution.

Investigational Device Exemption (IDE): permits a device, which otherwise would be required to comply with a performance standard or to have premarket approval, to be shipped lawfully for the purpose of conducting investigations of that device. An approved IDE means that the IRB (and FDA for SR devices) has approved the sponsor's (or sponsor-investigator's) application and that the study meets all the requirements under 21 CFR 812.

Investigational Drug or Agent: any pharmaceutical forms of a new drug/agent or biologic used in a clinical investigation. The terms include products that are not generally recognized as safe and effective for any use under the conditions prescribed, recommended, or suggested by the Food and Drug

Administration (FDA) or products already approved by the FDA as safe and effective that are being studied for new indications.

Investigational New Drug (IND): exemption to the Federal law that prohibits an unapproved drug from being transported across state borders. This exemption is required since in most cases the sponsor will need to ship the investigational drug to investigator.

Investigational Use: a clinical evaluation of a legally marketed device for a new intended use or a new indication for use.

Investigator (UK AR 7:2 Financial Conflicts of Interest in Research): the project director or principal investigator/program director, co-investigator, collaborator, senior/key personnel, faculty associate, and any other person, regardless of title or position, who is responsible for the design, conduct, reporting, or proposing of research.

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L

Legally Authorized Representative (LAR): an individual who has the authority to make research participation decisions on behalf of another.

Life-threatening (21 CFR 56.102(d)): diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted. Life-threatening situations include diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

Life-threatening event: any experience that places the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

Limited Data Set: a subset of identifiers that contain the following elements: city, state, zip code, date of birth, death, or date of service.

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M

Major Violation: one that may impact subject safety, make a substantial alteration to risks to subjects, or any factor determined by the IRB Chair or an IRB member to warrant a review of the violation by the convened IRB.

Medical Device: any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized.

Minimal Risk (HHS): 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 Violation: a violation that does not impact subject safety or does not substantially alter risks to subjects.

Modifications: changes that impact the overall protocol.

Multi-site research study: uses the same protocol to conduct non-exempt human subjects research at more than one site.

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N

Noncompliance: conducting research in a manner that disregards or violates federal regulations or institutional policies and procedures applicable to human research. Noncompliance with IRB policies and/or federal requirements may involve a range of issues from relatively minor, administrative, or technical violations to more serious violations which pose risk to subjects and/or violations of their rights and welfare.

Nonsignificant Risk (NSR) device study: one that does not meet the definition for an SR study.

Not Human Research (NHR) determination: official determination made by an IRB Chair or designee, ORI Director, or ORI Associate Director based on a proposed activity not meeting the federal definition of human subject and/or research. NHR does not require IRB review.

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P

Participant site: entity that will rely on the IRB of another institution/organization (a.k.a. an external IRB) to carry out the IRB review of human subjects research for a multi-site study.

Permission: the agreement of parent(s) or guardian to the participation of their child or ward in research or clinical investigation. Permission includes the element of consent set forth in federal regulations and outlined in the informed consent template included in the IRB expedited and full review applications.

Preparatory Work: PHI reviewed for the purpose of designing a research study or identifying potential subjects. PHI cannot be removed from the CE during the review.

Principal Investigator (UK): may be a UK employee, UK student, or in rare cases may be an employee at a site with which UK has signed an IRB Memorandum of Understanding, IRB Authorization or Individual Investigator Agreement.

Privacy: concerns people and their expectations of private information, settings, and situations.

Private information (HHS): 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 that has been provided for specific purposes by an individual will not be made public (e.g., a medical record).

Prospective research: evaluates data that does not yet exist at the time the protocol is submitted to the IRB for initial review

Protected Health Information (PHI): any of the 18 identifiers listed in the HIPAA Privacy Regulations in combination with health information that is created or maintained by a UK covered entity (CE) department that relates to the past, present, or future physical or mental health or conditions of an individual.

Protocol Violation: any exception or deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. These protocol violations may be major or minor violations.

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R

Related: In the opinion of the Principal Investigator, the experience was caused or possibly caused by the research procedures. If there is insufficient information to determine whether the internal event is related, it should be reported as it is related.

Relying IRB or Organization: is relying on the review of or has ceded IRB review to another IRB to provide oversight for a specific research study or set of studies. This process is also referred to as deferring IRB review.

Research (HHS): A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR 46.102(l)]. Activities that meet this definition constitute research, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Also, if a study involves human subjects (in accordance with the human subject definition below) and is being done for the purpose of completing an academic degree program (e.g., thesis, capstone, dissertation, etc.), it is considered by the university to meet the definition of research, whether designed to contribute to generalizable knowledge or not.

Research Involving a Human Being as an Experimental Subject (DoD): an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction [32 CFR 219.102(e)(1)(i)]. Research involving

a human being as an experimental subject is a subset of research involving human subjects. 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. This definition does not include activities that are not considered research involving human subjects, activities that meet exemption criteria, and research involving the collection or study of existing data, documents, records, or specimens from living individuals.

Research Monitor: an individual 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 expertise consistent with the nature of risk(s) identified within the research protocol, to protect the safety and well-being of human subjects.

Retrospective research: evaluates data that exists at the time the protocol is submitted to the IRB for initial review.

Reviewing IRB (also referred to as the IRB of record): the IRB that provides the ethical review of the research.

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S

Serious Disease: a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent.

Serious noncompliance: failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as:

- (1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or
- (2) Substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.

Severely Debilitating (21 CFR 56.102(d)): 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.

Significant financial interest: anything of monetary value, including, but not limited to:

- Salary or other payments for services (e.g., consulting fees or honoraria);
- Equity interests (e.g., stocks, stock options, or other ownership interests);
- A proprietary interest in the research such as a patent, trademark, copyright, or licensing agreements including royalties from such rights; • A financial interest in the sponsor, product or service being tested;

- A position as an executive director or director of the agency or company sponsoring the research regardless of the amount of compensation;
- Any compensation that could be affected by the outcome of the research regardless of the amount of compensation.

Significant financial interest does NOT include:

- Salary, royalties, or other remuneration from the University;
- Income from seminars, lectures, or teaching engagements sponsored by public or non-profit entities;
- Income from service on advisory committees or review panels for public or non-profit entities;
- An equity or financial interest that when aggregated for the IRB member or consultant and the IRB member's or consultant's spouse and dependent children meets both of the following tests: does not exceed \$5,000 in value as determined through reference to public prices or other reasonable measures of fair market value and does not represent more than a 5% ownership interest in any single entity;
- Salary, royalties or other payments that when aggregated for IRB member or consultant and the IRB member's or consultant's spouse and dependent children over the next 12 months are not expected to exceed \$5,000.

Significant Personal Interest: an interest that the IRB member or consultant believes conflicts with his/her ability to objectively review a protocol including interests of the individual or immediate family member (spouse and dependent children) involved in the design, conduct, or reporting of the research protocol.

Significant Risk (SR) device study: a study of a device that presents a potential for serious risk to the health, safety, or welfare of a participant and (1) is 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 prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

Sponsors: agencies, institutions, companies, organizations, foundations, or other grantors responsible for funding a research study. The term sponsor is understood to include any intermediaries, such as contract research organizations or coordinating centers, acting as agents of the sponsor in carrying out the responsibilities above. All research falling under these types of agreements are considered sponsored projects.

Subject: as defined in device regulations [21 CFR 312.3], a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.

Support of a study (DoD): the provision of at least a portion of the 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 DoD personnel as subjects, access to or information about DoD personnel for recruitment, identifiable data or specimens from living individuals, or the use of other DoD data resources.

Suspension of IRB approved research: a temporary interruption in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.

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T

Termination of IRB approval: a permanent halt in the enrollment of new subjects, activities involving previously enrolled subjects, or other research activities.

Treatment IND: a large scale expanded access program typically following resolution of phase III or during phase II where sufficient safety data is available.

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U

UK Covered Entity Department: any department that provides services that meets the definition of health care provider, health plan, or health care clearinghouse and bills patients/subjects electronically. UK legal counsel determined which UK departments fall within UK's CE.

Unacceptable Audit Finding (NCI Guidelines for Auditing Clinical Trials): includes multiple major deficiencies, a single major flagrant deficiency, or an excessive number of lesser deficiencies.

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 or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

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W

Waiver of Authorization: a request to forgo the authorization requirement based on the fact that the disclosure of PHI is a minimal risk to the subject and the research cannot practically be done without access to/use of PHI.

Waiver of Documentation: a request to waive the requirement to collect a signature to document that the informed consent process has occurred. There are three options under which this waiver can be considered.

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