

University of Arkansas - Fayetteville

Protection of Human Subjects in Research

Procedures Manual

Office of Research Compliance

Institutional Review Board

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# 1. Mission and Guiding Ethical Principles

The University of Arkansas is committed to ensuring that researchers use safe, ethical practices when engaging in human subjects research (HSR). In doing so, the University is guided by the ethical principles regarding human subject research as set forth in The Nuremberg Code and in the Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, titled *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (also known as the Belmont Report).

## 1.1 The Nuremburg Code

The Nuremburg Code was formulated during the war crimes trials following World War II and served as a standard for judging physicians and scientists who had conducted biomedical experiments on prisoners held in concentration camps. Widely adopted by investigators conducting studies on human subjects, the Nuremburg Code has served as a prototype for later codes, all of which are intended to ensure that research involving human subjects is carried out in an ethical manner.

 Tenets of the Nuremburg Code include:

1. Voluntary consent is essential.
2. The research should be expected to yield results for the good of society, unprocurable by other means or methods, and not be random or unnecessary in nature.
3. The research should be designed and based on the results of animal experimentation and on a knowledge of the nature and history of the disease or other problem under study so that expected results will justify the research.
4. Unnecessary physical and mental suffering and injury should be prevented.
5. No experiment should be conducted when there is a priori reason to believe that death or disabling injury may occur, except in those experiments in which research physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved.
7. Adequate facilities should be available and preparations made to protect subjects against even remote possibilities of injury, disability, or death.
8. Only scientifically qualified persons should conduct the research. The highest degree of skill and care should be required through the entire research study.
9. Research subjects should be at liberty to decline further participation if s/he has reached the physical or mental state at which continuation of the research seems to him/her impossible.
10. The researcher must be prepared to terminate the study at any stage if s/he has probable cause to believe, in the exercise of good faith, superior skill, and careful judgment, that continuation of the study is likely to result in injury, disability, or death of study subjects.

## 1.2 The Belmont Report

 The Belmont Report comprises three basic principles.

1. Respect for persons demands that individuals be treated as autonomous agents and that persons with diminished autonomy are entitled to protection. In practical terms, respect for persons demands that subjects enter into research voluntarily and with adequate information about the research situation and possible consequences.
2. Beneficence requires that research a) does not harm subjects, and b) maximizes the possible benefits and minimizes possible harms. Research may require exposing subjects to possible risk, and researchers must determine when the possible benefits of the research justify exposure to the potential risks.
3. Justice addresses the question of who ought to receive the benefits of research and who should bear its burdens. When publicly-supported research leads to the development of therapeutic devices and procedures, justice demands that these provide advantages to all, regardless of income level, and that such research should not unduly involve persons from groups unlikely to benefit from subsequent applications of the research.

# 2. Does this Policy Apply to my Protocol?

The University of Arkansas ensures that participants in HSR are treated ethically by its employees, students, and anyone using University facilities or resources. (See Department of Health and Human Services (HHS) 45 CFR Part 46, Protection of Human Subjects) and, when applicable, Food and Drug Administration (FDA), 21 CFR Part 50, Protection of Human Subjects and 21 CFR Part 56, Institutional Review Boards.)

Therefore, if an activity involves human subjects and is conducted by or under the supervision or control of university employees and/or students in connection with their responsibilities, whether on or off campus, then the *University of Arkansas Protection of Human Subjects in Research* Policy(HSR Policy) applies to it, and review and approval by the Institutional Review Board (IRB) may be required. This policy also applies to all HSR which is conducted by an external party on university property and/or using university facilities or resources.

The University of Arkansas HSR Policy applies to all projects regardless of funding source or status (*i.e*. unfunded research projects must still comply with Policy).

## What is a Human Subject?

HHS defines a human subject as “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 the information or biospecimens.” [45 CFR 46.102(e)]

The FDA defines a human subject as “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be a healthy human or a patient.” [21 CFR 50.3(g)]

## What is Research?

HHS defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(l)]

The FDA defines clinical investigation to be synonymous with research and 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, or 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.

# 3. Does my Protocol Require Review by the IRB?

Some protocols may involve human subjects but do not constitute “research” and are therefore not considered to meet the definition of Human Subjects Research. These protocols do not require IRB oversight and do not need to be submitted for review. Under the revised Common Rule [45 CFR 46.102(l)], effective January 21, 2019, the following activities will not be considered research:

1. Scholarly and journalistic activities (*e.g.* oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on specific individuals about whom the information is being collected.
2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. These activities are limited to those necessary to allow a public health authority to identify, assess, monitor, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance. This includes activities associated with providing timely situational awareness and priority setting during of an event or crisis that threatens public health.
3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or investigative purposes.
4. Authorized operational activities, determined by each agency, in support of intelligence, homeland security, defense, or other national security missions.

Examples of activities that do not meet the definition of research and therefore do not require review and approval by the IRB include:

* Data collection for departmental or other administrative purposes (*e.g.* teaching evaluations, customer service surveys)
* Information-gathering interviews with questions focusing on things, products, or policies.
* Class projects the purpose of which is to provide training in research methodology.
* Program evaluation/quality improvement/quality assurance projects.

# 4. Criteria a Protocol Must Meet for IRB Approval

Per 45 CFR 46.111, there are certain criteria that must be met for a protocol to be approved. These include:

* 1. Minimizing risks to the subjects by using procedures which are consistent with sound research design; do not expose subject to unnecessary risk; and where appropriate use procedures already being performed on the subjects;
	2. Ensuring that the risks to the subjects are reasonable in relation to the anticipated benefits to the subjects and the importance of the information to be gained;
	3. Selecting subjects in an equitable manner;
	4. Seeking and appropriately documenting legally effective, informed consent from each subject or from the subject’s legally authorized representative to the extent required by 45 CFR 46.116;
	5. Making adequate provisions, when appropriate, for monitoring the data collected to ensure the safety of the subjects;
	6. Providing adequate protection for the privacy of the subjects and maintaining the confidentiality of the data as appropriate; and
	7. Ensuring that appropriate additional protections are in place when some or all the subjects are members of vulnerable populations;
	8. Ensuring that the researchers have the resources necessary to protect participants, including time for research, number of qualified staff, and facilities.
	9. For the purpose of conducting a limited review for certain exempt categories of research, the IRB shall not be required to make the determinations listed in 1 – 6 above, but shall make the following determinations:
1. Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained, as applicable;
2. Broad consent is appropriately documented, or waiver of documentation is recorded, as appropriate; and
3. If a change is made for research purposes in the way identifiable private information or identifiable biospecimens are stored or maintained, there are sufficient provisions to protect privacy and maintain data confidentiality.

Note: Measures implemented to protect the privacy and confidentiality of participants will be done to the extent possible under Arkansas state law and applicable University policy.

# 5. Submitting your Protocol for Review & The IRB Process

If your proposed activity meets the definition of Human Subjects Research and does not otherwise fit into one of the categories described in Section 3, then your proposal will be subject to review by the IRB. There are three categories of IRB review: Exempt, Expedited, and Full Committee Review. When submitting your proposal in Streamlyne (formerly RazorGrant), you may select the type of review you think is appropriate for your proposal. You may access the [HSR decision charts](https://research.uark.edu/units/rscp/exempt-determination.php) to help you determine what kind of review will likely be required. This will be reviewed by the IRB Coordinator who will provide a final determination as to which type of IRB review is appropriate.

## 5.1 Exempt Categories of Research

Under the revised Common Rule, effective January 21, 2019 there are eight categories of exempt research [45 CFR 46.104(d)(1-8)].

### 5.1.1 Category 1: Research in Established or Commonly Accepted Educational Settings

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Research conducted in established or commonly accepted educational settings that specifically involve usual educational practices that are not expected to adversely affect students’ opportunity to learn required educational content; or assessment of educators providing instruction; is exempt from IRB review. Included is most research on instructional strategies; research on the effectiveness of instructional techniques; and comparison among instructional techniques, curricula, or classroom management strategies.

### 5.1.2 Category 2: Educational Tests, Surveys, Interviews, Observations of Public Behavior

Research that includes only interactions involving educational tests (cognitive, diagnostic, aptitude, achievement); survey procedures; interview procedures; or observations of public behavior (including visual or auditory recording) is exempt if at least one of the following criteria is met:

1. the information obtained is recorded by the investigator such that the identity of the participants cannot be readily determined, either directly or indirectly; or
2. any disclosure of participant responses outside the research would not be reasonably expected to place the participant at risk of criminal and/or civil liability or be damaging to the participant’s financial well-being; employability; educational advancement; or reputation; or
3. the information obtained is recorded by the investigator such that the identity of participants can be readily determined, and an IRB conducts a limited review to make the determination as per 45 CFR 46.111(a)(7).

### 5.1.3 Category 3: Benign Behavioral Interventions and Collection of Information from Adult Subjects

Research involving benign behavioral interventions in conjunction with the collection of information from adult subjects through verbal and/or written responses (including data entry) or audiovisual recording if the participant agrees to the intervention and collection of information is exempt if at least one of the following criteria is met:

1. the information obtained is recorded by the investigator such that the identity of the participants cannot be readily determined, either directly or indirectly; or
2. any disclosure of participant responses outside the research would not be reasonably expected to place the participant at risk of criminal and/or civil liability or be damaging to the participant’s financial well-being; employability; educational advancement; or reputation; or
3. the information obtained is recorded by the investigator such that the identity of participants can be readily determined, and an IRB conducts a limited review to make a determination as per 45 CFR 46.111(a)(7)

Benign behavioral interventions are:

* brief in duration;
* harmless;
* painless;
* not physically invasive;
* not likely to have a significant, lasting impact on the subject;
* not expected to cause offense or embarrassment to the participant.

Research that involves deceiving participants as to the nature or purpose of the research are not exempt unless the subject agrees to participate in research involving circumstances in which s/he will be informed that s/he will not be aware of the true nature or purpose of the research.

### 5.1.4 Category 4: Secondary Research for Which Consent is Not Required

Secondary research uses of private, identifiable information or identifiable biospecimens, are exempt if at least one of the following criteria is met:

1. the private, identifiable information or identifiable biospecimens are publicly available; or
2. information is recorded by the investigator such that the identity of the subjects cannot be readily ascertained directly or indirectly, and the investigator neither contacts the subjects nor reidentifies them; or
3. the research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is 45 CFR 160 and 164, subparts A and E for health care operations or research as defined in 45 CFR 164.501 or for public health activities and purposes as described in 45 CFR 164.512(b); or
4. the research is conducted by or on behalf of a federal agency or department using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained in formats subject to and in compliance with federal statutes.

This exemption does not apply to the primary collection of information and/or biospecimens.

### 5.1.5 Category 5: Research and Demonstration Projects Conducted or Supported by a Federal Department or Agency

Research and demonstration projects conducted or sponsored by a federal agency or department, or otherwise subject to the approval of agency or department heads, are exempt. This exemption applies to activities whose purpose includes the study, evaluation, improvement, or examination of public benefit or service programs. These include, but are not limited to, procedures for obtaining benefits or services under those programs; changes in or alternatives to those programs or procedures; or changes in methods or levels of payment for benefit or services under those programs.

Each federal agency or department must establish a list of the research and demonstration projects that agency or department conducts or sponsors that are subject to this exemption; that list must be publicly accessible on a website or through other means. The research or project must be published on this list prior to the initiation of the research or project.

### 5.1.6 Category 6: Taste and Food Quality Evaluation and Consumer Acceptance Studies

This exemption applies if wholesome foods without additives are consumed, or if the food being consumed contains ingredients at or below levels and for uses found to be safe; or contains agricultural, chemical or environmental contaminants at or below levels found to be safe as determined by the Food and Drug Administration (FDA) or approved by the Environmental Protection Agency (EPA) or the United States Department of Agriculture’s (USDA) Food Safety and Inspection Service.

### 5.1.7 Storage or Maintenance for Secondary Use for Which Broad Consent is Required

This exemption allows for the storage of data and/or specimens in a repository, with identifiers maintained, that were collected under an approved IRB protocol with Broad Consent for future secondary use. This is a new exemption category in the revised Common Rule. The IRB must conduct a limited review and make the determination required by 45 CFR 46.111(a)(8).

### 5.1.8 Secondary Research for Which Broad Consent is Required

This exemption allows for secondary research use/analysis of identifiable data and/or biospecimens that were collected under an approved IRB protocol with Broad Consent. This is a new exemption category in the revised Common Rule.

Under this exemption, the following criteria must be met:

1. Broad consent for the storage, maintenance, and secondary research use of identifiable private information or biospecimens was obtained; and
2. Documentation of informed consent or waiver of such documentation was obtained; and
3. The IRB conducts a limited review and determines that the proposed secondary research is within the scope of the broad consent; and
4. The researcher does not include returning individual results to study participants as part of the study plan.

A limited review, when required, must be conducted by the IRB Chair or another experienced member of the IRB. The member conducting the limited review may either approve the protocol or refer it to the full board for consideration. S/he may not disapprove a protocol.

## 5.2 IRB Exemption Review

If your protocol fits into one of the categories above, you may select “Exempt” under Protocol Type when submitting your proposal through the Streamlyne system. The IRB Coordinator will review the submission and provide a final determination within one week of receipt of your submission.

If you are notified that your protocol is Exempt, you may immediately begin activities on your protocol. Documented (*i.e.* written or witnessed) informed consent of research participants is not required for activities designated “Exempt.” However, for protocols other than those meeting existing data exemption criteria, the University of Arkansas requires that, at a minimum, all research participants be informed of the following:

1. the name(s) and contact information for the principal investigator(s), including Faculty Supervisor if applicable, for someone to contact with any questions about the research; and
2. the purpose of the research activity; and
3. a description of what you are asking your participant to do, including approximately how long it will take; and
4. a statement that participation is voluntary, and that refusal, for any reason, to participate will not adversely affect any other relationship with the University, the researchers, and/or any third party (*e.g.* a sponsor or business entity); and
5. contact information for the Office of Research Compliance to allow participants to obtain additional information about the rights of research subjects.

NOTE: For studies involving minors (those under the age of 18), the IRB, at its discretion, may require additional elements be included.

## 5.3 IRB Expedited Review

Certain categories of research may be reviewed by the IRB through an Expedited process. These categories are for research protocols involving no more than minimal risk to the subjects or for minor changes to previously approved protocols. [45 CFR 46.110] The [list of eligible research categories](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html) is periodically updated by HHS and is published in the Federal Register. Any research not on this list may not be reviewed through the Expedited process. Research protocols involving prisoners may not be reviewed through the Expedited process.

Research Categories Eligible for Expedited Review:

1. Clinical studies of drugs and medical devices when either (a) or (b) is met:
	1. Research on drugs for which an INDA [21 CFR Part 312] is not required; or
	2. Research on medical devices for which (i) an investigational device exemption application is not required; or (ii) the medical device is cleared/approved for marketing and the device is being used as approved.
2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture
	1. From healthy, nonpregnant adults weighing at least 110 pounds (amount collected may not exceed 550 mL in an 8-week period, with no more than two draws per week); or
	2. From other adults and children, taking into consideration their age, weight, and health; collection procedures; amount of blood to be collected; and frequency of collection. Blood may be drawn no more than twice per week and the volume collected may not exceed the lesser of 50 mL or 3 mL/kg body mass in an 8-week period.
3. Prospective collection of biological specimens for research purposes by non-invasive means.
4. Collection of data through non-invasive procedures, not involving sedation or general anesthesia, routinely employed in clinical practice. Procedures involving X-rays or microwaves are excluded. If medical devices are used, they must be cleared and/or approved for marketing.
5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected, solely for non-research purposes (*e.g.* medical diagnosis or treatment).
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior. Some research in this category may be qualify for an exemption from IRB review and approval.
8. Continuing review of research previously approved by the IRB as follows:
	1. Where (i) the research is permanently closed to enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
	2. Where no subjects have been enrolled and no additional risks have been identified; or
	3. Where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an INDA or investigational device exemption, where the preceding categories of research eligible for expedited review do not apply but the IRB has determined and documented that the research involves no greater than minimal risk and no additional risks have been identified.

Protocols qualifying for Expedited review will be assigned to an experienced voting member of the IRB who has served on the committee for at least one year.

No IRB member will be asked to review a protocol in which s/he has an actual or perceived conflict of interest. Conflict of Interest and Conflict of Commitment are defined in [University Policy 404.0](https://vcfa.uark.edu/policies/fayetteville/vprs/4040.php). Common examples of conflicts which would disqualify an IRB member from reviewing a particular protocol include, but are not limited to, situations in which the reviewer:

* has a financial conflict of interested as defined in the University policy;
* has a working relationship with the researcher(s) named on the protocol (*e.g.* researchers and reviewer both work in the same department);
* is an immediate family member of the researcher;
* is named on and has some role in the protocol;
* is involved in any collaborative relationship with the researcher.

If the IRB member feels s/he has an actual or perceived conflict of interest for an assigned protocol, the protocol will be assigned to another member.

If the member conducting an Expedited review does not feel that the protocol may be approved, s/he will refer the protocol to the full committee. Protocols may not be disapproved through the Expedited Review process. If a protocol is approved through the Expedited Review process, all IRB members will be notified, in writing, of the decision.

The duties of the Expedited Reviewer include the following:

1. reviewing all materials, including grant protocols, if applicable, related to the assigned protocol;
2. informing the IRB Coordinator that additional information, expertise, or consultation is required;
3. asking questions of the Principal Investigator and/or other subject matter experts to conduct a thorough review and providing clear instructions regarding recommendations, required modifications, and/or the need for further information and/or clarification(s);
4. determining whether the protocol meets the criteria for IRB approval; and
5. providing notice, through Streamlyne, of his/her decision to either approve the protocol or refer it to the full IRB for further consideration.

Once a protocol has been approved through the Expedited Review process and notice has been given to the researcher by the IRB Coordinator, work under that protocol may begin.

## 5.4 Full IRB Review

If a protocol requires review by the full IRB, it will be added to the agenda for the next scheduled meeting. The researcher will be notified of the meeting time and location. Either the Principal Investigator or a co-researcher is required to attend the meeting to answer questions or address concerns of the IRB.

## 5.5 Medical or Psychological Emergency Situations – Can a Protocol be Initiated Prior to Approval by the IRB?

Under no circumstances may research activities be initiated prior to review and approval by the IRB, even in extenuating circumstances such as a medical emergency. Whenever emergency care is initiated prior to IRB review and approval, the patient may **not** be considered a research subject. See [OHRP Guidance, *Human Subject Protections – Emergency Medical Care* No. 91-01.](https://www.hhs.gov/ohrp/regulations-and-policy/guidance/emergency-medical-care-and-research/index.html)

Under 45 CFR 46.116(j), nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state or local law.

## 5.6 Frequency of IRB Meetings to Review Protocol Submissions

During the academic year, the IRB meets monthly, or as otherwise needed, to review protocols and conduct other business. During the summer semester, the IRB will meet as needed, provided that a quorum of voting members is available. In no event will there be fewer than two scheduled meetings of the IRB during the academic year.

An IRB meeting is properly convened and thus able to conduct official business, including the review and approval of protocols, when there is a quorum of members present. A quorum requires a simple majority of voting members (i.e. 50% + 1). Non-voting members do not count towards a quorum. Members who are on leave or sabbatical are not counted when determining the number of members who must be present at a meeting to make quorum. One non-scientist member must be present to meet quorum. No deliberation or action requiring a vote may begin until a quorum is established. A Meeting Attendance Sheet will be circulated to record the establishment of a quorum. The IRB Chair or his/her designee will determine if a quorum has been established at the beginning of the meeting and throughout the meeting as necessary.

If a member must leave the meeting for any reason, including to avoid conflicts of interest, the Chair will confirm that a quorum still exists before proceeding.

## 5.7 Avoiding Conflicts of Interest/Commitment

Per 45 CFR 46.107(d), any IRB member with a conflict of interest in a proposal subject to review is prohibited from participating in the review, deliberation of, and voting on that protocol, except to provide information as requested by the IRB. Conflicts of Interest and Conflicts of Commitment are defined in [University Policy 404.0](https://vcfa.uark.edu/policies/fayetteville/vprs/4040.php).

At the beginning of each meeting the IRB Chair will remind members of this policy and document any actions taken during that meeting to avoid conflicts. These actions may include:

* excluding IRB members with conflicts from discussion or voting on a particular protocol;
* asking IRB members with conflicts to leave the room during deliberation or voting on that protocol; and
* removing IRB members from the quorum count for that protocol.

The IRB Chair or his/her designee will also determine if there is a conflict for any consultants participating in the meeting. If a consultant is determined to have a conflict, s/he may not provide information on that protocol and may not be present during deliberation and voting on that protocol.

## 5.8 Determinations

Following presentation and discussion of a given protocol, the IRB will vote. The IRB may take the following actions:

1. Vote to approve the protocol with no modifications and/or clarifications\*;
2. Vote to approve the protocol but with modifications and/or clarifications\*; or
3. Vote to disapprove the protocol.

\* Protocol approvals are granted for one year.

Notification of the results of the IRB vote will be sent to investigators by the IRB Coordinator via the Streamlyne system.

## 5.9 Appealing a Protocol Decision

If the IRB disapproves a protocol, the researcher may submit a written request to the IRB Coordinator to appeal the disapproval. The request should be submitted no later than one week after receiving notice of disapproval. It will then be placed on the schedule and the researcher will be asked to appear before the IRB in person at the next regularly scheduled meeting.

## 5.10 Continuing Review

### 5.10.1 Initial Approval Period

If your protocol is determined to be exempt, it will be approved for an indefinite period subject to any changes which you may wish to initiate.

If your protocol is approved through Expedited Review, it is approved for one year. If your protocol required review by the Full Board, it will be approved for a maximum time of one year from the date of IRB approval meeting in accordance with 45 CFR 46.109(e). Shorter approval periods may be required for projects where the degree of risk warrants additional oversight.

In the case of protocols reviewed and conditionally approved by the full IRB, the approved research period begins on the date that the required changes are received, reviewed, and approved, not the date on which the conditions are met by you. You are not authorized to begin your research until you have received an Approval Letter through the Streamlyne system.

Regardless of the protocol expiration date, you must get IRB approval prior to initiating changes in the approved research.

### 5.10.2 What to do if the Protocol Continues Beyond the Initial Approval Period

As stated above, if your research is determined to be exempt it is approved for an indefinite period and will not require additional review unless you modify the protocol.

Per 45 CFR 46.109(f), continuing review is not required in the following circumstances, unless the IRB determines otherwise:

* Research eligible for expedited review [see 45 CFR 46.110];
* Research reviewed by the IRB in accordance with the limited review described in 45 CFR 46.104(d);
* Research that has progressed to the point that it involves only a) data analysis, including analysis of identifiable private information or identifiable biospecimens; and/or b) accessing follow-up clinical data from procedures that research subjects undergo as part of clinical care.

If continuation of the research is not approved prior to the expiration date, you must halt all research and may not enroll further participants until a full protocol has been submitted for appropriate review and approval. **There are no exceptions!**

## 5.11 Modifications to Approved Protocols

If a researcher wants to modify an approved Exempt protocol in a way that may affect the level of risk to the participants, s/he must notify the IRB of the requested amendment through the Streamlyne system prior to initiating any changes.

If a researcher wants to modify research which has been approved by Expedited or Full Review, s/he must submit an Amendment Request through the Streamlyne system and receive approval prior to modifying any aspect of the previously approved protocol.

## 5.12 Meeting Minutes

Pursuant to 45 CFR 46.115 and OHRP recommended procedures, IRB minutes will contain adequate detail to document the following for a proposed protocol:

* Attendance at the meeting or portions of the meeting
* Separate deliberations, actions, and votes for each protocol undergoing initial or continuing review by the convened IRB
* The vote on all IRB actions, including the number of members voting for, against, and abstaining
* The basis for requiring changes in research
* The basis for disapproving research
* A written summary of the discussion of controverted issues and their resolution
* For initial and continuing review, the approval period
* If the approval period is less than a year, documentation of IRB determinations regarding the risk and the approval period
* The name(s) of IRB members who left the meeting due to a conflict of interest, the fact that a conflict of interest was the reason for the absence, and the continued existence of a quorum during their absence
* Protocol-specific determinations required by the regulations and findings justifying those determinations for:
* Research involving pregnant women, fetuses, and neonates
* Research involving prisoners
* Research involving children
* Adults with diminished decision-making capacity
* Required findings under 45 CFR 46.116(e - f) when approving any waiver or alteration of the consent procedure requirements

## 5.13 IRB Records and Record Retention

In addition to the IRB Meeting Minutes, the IRB Records will include the following information to meet the requirements of 45 CFR 46.115(a):

* Copies of all research protocols reviewed, including approved sample consent documents
* Expert consultant evaluations, if included with a protocol
* Progress reports submitted by researchers
* Reports of unanticipated problems or adverse events involving participants
* Records of continuing review activities
* Correspondence between the IRB and researcher
* Statements of significant new findings provided to participants.
* For initial and continuing review of research by the expedited procedure:
* The specific permissible category
* Description of action taken by the reviewer
* Any findings required under the regulations
* For exemption determinations, the specific category of exemption

Pursuant to 45 CFR 46.115(b), the IRB will retain IRB Minutes and Records as follows:

* IRB records relating to research are retained for a minimum of three years after the completion of a project and any additional period required by the sponsor.
* IRB records are accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.
* If a protocol is cancelled without subject enrollment, IRB records are maintained for at least three years after cancellation.
* Records are maintained in a way that ensures participant confidentiality.
* IRB records for a protocol are organized to allow a reconstruction of a complete history of IRB actions related to the review and approval of the research protocol.

# 6. Data and Safety Monitoring Plans

University of Arkansas researchers are responsible for monitoring the safety of their research study participants. The Office of Human Research Protections (OHRP) recommends that the IRB also considers setting up a monitoring plan for protocols when deemed appropriate. The IRB will consider this on a case-by-case basis, including when a project:

* is particularly complex and involves unusual levels or types of risks to study subjects;
* involves vulnerable populations;
* is conducted by a researcher who has previously failed to comply with IRB determinations; or
* is found, through continuing review or from reports from other sources, to involve protocol changes that were not approved by the IRB.

The IRB may, at its discretion, choose a project at random for monitoring.

# 7. Unanticipated Problems and Previously Unknown Risks

Per 45 CFR 46.108(a)(4)(i), if an unanticipated problem arises or you become aware of any information during the study that involves new or previously unrecognized risks to study participants or others, you must report this to the IRB as soon as possible, but no later than two working days after you become aware of the event or information. You must submit an Unanticipated Problems report via the Notify IRB action in the Streamlyne system within five working days of identification of the event or information.

The OHRP generally considers unanticipated problems to include any incident, experience or outcome that meets **all** the following criteria:

* unexpected in terms of its nature, severity, or frequency given the protocol and characteristics of the subject population; and
* related or possibly related to participation in the research (*i.e.* there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures used in the research); and
* puts participants or others at a greater risk of harm than originally anticipated, including physical, psychological, economic, or social harm.

Upon receipt of the Unanticipated Problems report, the IRB Coordinator, IRB Chair, and/or the Director of Research Compliance will determine if the issue warrants further investigation requiring the full IRB’s review. All events meeting these criteria will be reported in accordance with OHRP requirements and other applicable federal regulations and sponsor guidelines.

# 8. Legally Effective Informed Consent Process

One of the three principle tenets of the [Belmont Report](https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html) is “Respect for Persons.” Respect for persons requires that 1) “individuals …be treated as autonomous agents” and 2) “persons with diminished autonomy are entitled to protection.” Thus, any human participants in a study “must enter into that research voluntarily and with adequate information.” The federal requirements of the legally effective informed consent process help ensure that a protocol meets this requirement of respect for persons.

An informed consent process must contain the following safeguards as required by 45 CFR 46.116(a), unless they are specifically waived by the IRB:

* The prospective subject or his/her legally authorized representative must have sufficient opportunity to consider whether to participate;
* The possibility of coercion or undue influence must be minimized to the extent possible;
* The process must contain the basic elements and other elements required by federal regulations and the IRB;
* The researcher or other designated individual communicating the information to prospective participants will provide that information in language understandable to the participants or their legally authorized representatives;
* Except in cases involving broad consent, informed consent must begin with a concise and focused presentation of key information most likely to assist someone in deciding whether or not to participate in the study;
* Except in cases involving broad consent, information must be presented in sufficient detail and must be organized and presented in a way that facilitates understanding; a list of unrelated facts does not meet this requirement;
* Exculpatory language through which the participant or his/her legally authorized representative is made to waive or appear to waive any of his/her legal rights will not be used;
* Exculpatory language through which the participant or his/her legally authorized representative releases or appears to release the researcher, sponsor, the investigative site, or its agents from liability for negligence will not be used;
* The researcher or the individual administering the consent process will give the participant or his/her representative adequate opportunity to read the entire consent form before signing;
* The participant or his/her representative will sign and date the consent form; and
* A copy of the signed consent form will be provided to the participant or his/her representative.

## 8.1 Basic Elements of Legally Effective Informed Consent

The informed consent process must provide each participant or his/her legally authorized representative with all the following elements of 45 CFR 46.116(b), unless specifically waived by the IRB:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

(9) One of the following statements about any research involving the collection of identifiable private information or identifiable biospecimens:

a) A statement that identifiers may be removed from identifiable private information or identifiable biospecimens and that, following such removal, the information or biospecimens may be used for future research studies or distributed to other researchers for future studies without additional consent; or

b) A statement that the subject’s information or biospecimens will not be used or distributed for future research studies.

## 8.2 Additional Requirements for Informed Consent

If the IRB deems it necessary, additional elements may need to be included in the informed consent process, per 45 CFR 46.116(c). These elements include:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the research which may relate to the subject's willingness to continue participation will be provided to the subject; and

(6) The approximate number of subjects involved in the study.

As applicable, the following elements may be required:

(7) A statement that the subject’s biospecimens (even if de-identified) may be used for commercial profit and whether the subject shall share in such profits;

(8) A statement as to whether clinically relevant research results, including individual results, will be disclosed to subjects and under what conditions; and

(9) For research involving biospecimens, whether the research will or might include whole genome sequencing.

The IRB will determine whether some or all the above additional elements must be included as part of the informed consent process for a particular study. The IRB will make this determination based on the nature of the research and its knowledge of the local research context. Pursuant to OHRP recommendations, if the IRB determines that additional elements are appropriate to the research study, this additional information will be considered just as essential as the basic elements of informed consent required by 45 CFR 46.116(a).

The IRB may require that additional information beyond the basic and additional elements be given to subjects during the informed consent process, when in the IRB’s judgment the additional information would meaningfully add to the protection of the rights and welfare of the subjects pursuant to 45 CFR 46.109(b).

The IRB may also determine that it is necessary to observe the consent process to protect the participants. In the event of that decision, researchers will work with the IRB to determine the best mechanism for this observation.

## 8.3 Requests for Waivers of or Alterations to the Required Elements for Informed Consent

Under 45 CFR 46.116 (e - f), the IRB may waive the requirement for informed consent or approve a consent procedure which does not include, or which alters, some or all the elements of informed consent set forth above, provided the IRB finds and documents that:

(1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (a) public benefit or service programs; (b) procedures for obtaining benefits or services under those programs; (c) possible changes in or alternatives to those programs or procedures; or (d) possible changes in methods or levels of payment for benefits or services under those programs; and

(2) The research could not practicably be carried out without the waiver or alteration. Under 45 CFR 46.116(e - f), the IRB may waive the requirement for informed consent or approve a consent procedure which does not include, or which alters, some or all the elements of informed consent set forth above, provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The research could not practicably be carried out without the waiver or alteration;

(3) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

(4) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

(5) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

## 8.4 Screening, Recruiting, or Determining Eligibility

The IRB may approve a project in which the researcher will obtain information or biospecimens for the purpose of screening, recruiting, or determining eligibility for prospective subjects, without obtaining informed consent from the subject or his/her legally authorized representative, if:

1. the researcher obtains the information or biospecimens through oral or written communication with the prospective subject or his/her legally authorized representative; or
2. the researcher will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

## 8.5 Posting of Clinical Trial Consent Form

Researchers must post the consent forms for any clinical trial conducted or supported by a federal department or agency on a publicly accessible federal website. The consent form must be posted after recruitment for the clinical trial has closed, and no later than 60 days after the last study visit by any research subject. Certain information may require redaction based on a determination made by the federal department or agency supporting or conducting the trial.

## 8.6 University of Arkansas Minimum Information Requirements for All Projects

Even if your project qualifies for a waiver of the informed consent process, all participants in your protocol must still be informed of the following:

1. the name(s) and contact information of the principal researcher(s), including Faculty Supervisor if applicable, for someone to contact with any questions about the research;
2. the purpose of the research activity;
3. a description of what you are asking your participant to do, including approximately how long it will take;
4. a statement that participation is voluntary, and that refusing, for any reason, to participate will not adversely affect any other relationship with the University, the researchers, and/or any third party (such as a sponsor or business entity); and
5. contact information for the IRB Coordinator to allow participants to get additional information about the rights of research subjects.

##  8.7 Additional Requirements for Vulnerable Populations

If your protocol involves children, pregnant women, prisoners, or adults unable to consent, you are required to take additional precautions in the consent process in accordance with 45 CFR 46 subparts B – D.

### 8.7.1 Children

Federal regulations permit the IRB to approve a research project involving children only after determining which of the following categories applies, and only if the project satisfies all the conditions in the applicable category:

1. Research that does not involve greater than minimal risk.

Pursuant to 45 CFR 46.404, this research may be approved if the IRB finds that adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

The IRB may determine that permission of one parent or guardian is sufficient. [45 CFR 46.408]

1. Research involving greater than minimal risk but presenting the prospect of direct benefit to an individual subject, or a monitoring procedure that is likely to contribute to the subject's well-being.

Pursuant to 45 CFR 46.405, this research may be approved if the IRB finds that the risk is justified by the anticipated benefit to the subject; the relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

The IRB may determine that permission of one parent or guardian is sufficient. [45 CFR 46.408(b)]

1. Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition

Pursuant to 45 CFR 46.406, this research maybe approved if the IRB finds that:

a)the risk represents a minor increase over minimal risk;

b)the intervention or procedure presents experiences to subjects that are reasonablycommensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

c)the intervention or procedure is likely to yield generalizable knowledge about thesubject's disorder or condition which is of vital importance for the understanding oramelioration of the subject's disorder or condition; and

d)adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

The IRB requires that permission of both parents is obtained, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child. [45 CFR 46.408(b)]

1. Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children

Pursuant to 45 CFR 46.407, this research may be approved if theIRB and the Secretary of HHS, after consultation with a panel of experts in pertinent disciplinesand following an opportunity for public review and comment, find that:

1. the research in fact satisfies 45 CFR 46.404, 46.405. or 46.406; or
2. the research presents a reasonable opportunity to further the understanding, prevention, oralleviation of a serious problem affecting the health or welfare of children; and
3. the research will be conducted in accordance with sound ethical principles; and
4. adequate provisions are made for soliciting the assent of children and the permission of theirparents or guardians

The IRB requires that the permission of both parents be obtained, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child. [45 CFR 46.408(b)]

1. Children who are wards of the state, or any other agency, institution, or entity can only be included in research in this category if the research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If one of these criteria is met and the research is approved, the IRB must require appointment of an advocate for each child who is a ward in addition to the person acting as guardian or in loco parentis. One person may serve as the advocate for multiple wards, however this advocate must have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child‘s participation in the research and cannot be associated in any way (except as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization. [45 CFR 46.409]

Unless these additional determinations have been made, in response to the initial submission and a clear statement that the research may involve Wards of the State, University of Arkansas investigators are not to enroll a Ward of the State onto a research project without first obtaining approval for a revision to the protocol. The IRB approved consent documents will include provisions for the signature of the advocate for the children.

### 8.7.2 Child’s Assent

Pursuant to 45 CFR 46.402 and 45 CFR 46.408, when children are the subjects of research and can provide assent, you must receive the assent of the child in addition to the permission of the parent(s). This means that the child should actively show his or her willingness to participate in the research. Mere failure to object cannot be construed as assent.

The IRB has the discretion to judge the children’s capacity to assent for all children in a proposed protocol, or on an individual basis. In judging capacity to assent, the IRB will consider the nature of the proposed activity, the ages, maturity, and psychological state of the children.

Pursuant to 45 CFR 46.408(a), the requirement of assent from children can only be waived by the IRB if:

* The children are not capable of providing assent, based on the age, maturity, or psychological state; or
* The capability of the children is so limited that they cannot reasonably be consulted; or
* The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research; or
* The assent can be waived using the criteria for waiver of the consent process.

### 8.7.3 Pregnant Women and Fetuses

Pursuant to 45 CFR 46.204, the IRB may approve research involving pregnant women or fetuses if all the following conditions are met:

a) where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and

b) the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means; and

c) any risk is the least possible for achieving the objectives of the research; and

d) if the research holds out the prospect of direct benefit to the pregnant woman, the prospect of direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the woman’s consent is obtained OR

e) if the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;

f) each participant providing consent under (d) or (e) is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and

g) for children who are pregnant, assent and permission are obtained in accord with the regulations for children in research; and

h) no inducements, monetary or otherwise, will be offered to terminate a pregnancy; and

i) individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

j) individuals engaged in the research will have no part in determining the viability of the neonate.

### 8.7.4 Neonates

*Nonviable neonates and neonates of uncertain viability.*

Pursuant to 45 CFR 46.205(a), neonates of uncertain viability and nonviable neonates may be involved in research if all the following conditions are met:

a) where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;

b) each participant providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;

c) individuals engaged in the research will have no part in determining the viability of the neonate;

d) the requirements regarding neonates of uncertain viability (see below) or nonviable neonates (see below) have been met as applicable.

*Neonates of uncertain viability*

Pursuant to 45 CFR 46.205(b), until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met:

(1) The IRB determines that:

(i) the research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or

(ii) the purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research, and

(2) the legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent‘s legally authorized representative is obtained (except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest).

*Nonviable neonates.*

Pursuant to 45 CFR 46.205(c), after delivery nonviable neonates may not be involved in research unless all the following additional conditions are met:

(1) vital functions of the neonate will not be artificially maintained;

(2) the research will not terminate the heartbeat or respiration of the neonate;

(3) there will be no added risk to the neonate resulting from the research;

(4) the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

(5) the legally effective informed consent of both parents of the neonate Is obtained (note: waiver or alteration of the consent does not apply here) If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of the legally authorized representative of either or both parents of a nonviable neonate will not suffice to meet the requirements.

*Viable neonates*.

Pursuant to 45 CFR 46.205(d), a neonate, after delivery, that has been determined to be viable may be included in the research only to the extent permitted by and in accord with the requirements for children involved in research.

*Research Making Post-Delivery Use of the placenta, the dead fetus, or fetal material*

Pursuant to 45 CFR 46.206, Research involving human fetal tissue (placenta, or tissue from a spontaneous or induced abortion or from a still birth) is evaluated as tissue specimen research, using the guidelines for research involving specimens. Studies using human fetal tissue for transplantation research and studies of human embryos involve very explicit regulations concerning consent and study procedures.

If you wish to conduct transplantation research with human fetal tissue you should contact The Office of Research Compliance well in advance of IRB application submission to schedule one or more meetings with representatives from the IRB, and General Counsel‘s office to discuss applicable federal and state regulations.

*Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates*

The IRB may approve research of this category only if the following requirements of 45 CFR 46.207 are met:

1. the research in fact satisfies 45 CFR 46.204; or
2. the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and
3. the research will be conducted in accordance with sound ethical principles; and
4. a legally effective informed consent will be obtained

### 8.7.5 Prisoners

Because incarceration could affect a person's ability to make a truly voluntary decision whether to participate in research, the federal regulations provide additional safeguards for the protection of prisoners.

At the University of Arkansas, any project that recruits prisoners must be reviewed at a full IRB meeting with a prisoner advocate present. If the project was not initially approved to recruit prisoners, then the investigator may not enroll a prisoner. The prisoner rules also apply for a subject who later becomes a prisoner, because it is unlikely that the IRB review of the research project contemplated the constraints imposed by incarceration.

Therefore, if you determine that a subject has become a prisoner at some later date after enrollment, and the study involves additional research interventions or interactions with that subject, the subject must either be dropped from follow-up, or you must submit an Amendment to the protocol in the Streamlyne system.

*Pursuant to 45 CFR* 46.*305, when a prisoner is a subject, in addition to the usual criteria for approval, the IRB must find that all the following safeguards are met:*

1) the research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);

2) any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

3) the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

5) the information is presented in language which is understandable to the subject population;

6) adequate assurance exists that parole boards will not consider a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole;

7) where the Board finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, considering the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

Additionally, the Informed Consent Document must include additional information for potential subjects regarding the fact that participation or non-participation will have no effect on the duration or terms of incarceration.

### 8.7.6 Other Vulnerable Populations

Individuals other than pregnant women, neonates, children, and prisoners may also be categorized as vulnerable to coercion or undue influence, and therefore require additional protection. Pursuant to 45 CFR 46.111(b), these include mentally disabled persons and economically or educationally disadvantaged persons. The OHRP also requires that any individual with diminished decision-making capacity be considered vulnerable. Examples of individuals with diminished decision-making capacity include, but are not limited to, trauma-induced impairments, mental retardation, and some forms of mental illness or dementia, whether temporary, progressive or permanent.

If your research involves a potentially vulnerable population, the IRB will consider what, if any, additional protections are warranted for the subjects in your study.

## 8.8 Informed Consent Documentation

The informed consent process must be documented pursuant to 45 CFR 46.117. Subject to any waiver or alteration as referenced above, the informed consent of the participant must be gained by one of the following methods:

1. a written consent document that contains the required elements of informed consent. This form may be read to the subject or the subject's legally authorized representative. The researcher must give either the subject or the representative adequate opportunity to read it before it is signed and dated; or
2. a short, written consent document stating that the required elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. This method requires a witness to the consent process and an IRB approved written summary of what is to be said to the subject or the representative. The short form itself must be signed and dated by the subject or the representative. The witness must sign both the short form and a copy of the summary, and the person actually obtaining consent must sign a copy of the summary. A copy of the summary must be given to the subject or the representative, in addition to a copy of the short form.

Your request to waive the use of a signed and dated consent form may only be approved by IRB if:

1. the only record linking the subject and the research is the consent document and the principal risk is the potential harm resulting from a breach of confidentiality. Each subject must be asked whether she/he wants documentation linking her/him with the research, and the subject's wishes will govern; or
2. the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

## 8.9 Limitations on the Requirements for Informed Consent under Other Federal, State or Local Laws.

Under 45 CFR 46.116(i), the informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed for informed consent to be legally effective.

Under 45 CFR 46.116(j), nothing in this policy is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.

# 9. University of Arkansas Protection of Human Subjects in Research: Responsibilities

## 9.1 Principal Investigators

The Principal Investigator has primary responsibility for assuring the day-to-day protection of the rights and welfare of research participants. All researchers are responsible for:

* research design;
* adhering to codes of ethics; applicable federal, state, and local laws and regulations; and applicable policies and procedures of the University, any sponsoring agency, and any cooperating institutions;
* training and supervising staff and students assisting in the research;
* obtaining informed consent from research participants;
* fully disclosing the research protocol and potential risks to research participants and complying with the requirements of the IRB to minimize risk to research participants;
* retaining records relating to their research for a minimum of three years after the completion of the project, and for any additional period required by the project sponsor;
* obtaining prior approval of the IRB to initiate the research and/or any changes in approved research protocols involving human subjects;
* reporting promptly to the IRB any unanticipated problems involving research participants which are, or may reasonably through to be, related to the research activities; and
* reporting any potential conflicts of interest or commitment in accordance with University Policy 404.0.

## 9.2 Unit Executive Officer

The Unit Executive Officer may be a College Dean, Department Chair, or other administrative person. S/he is responsible for:

* assuring that faculty, staff, and students in the Unit are kept informed of University policies and procedures, and of their responsibilities for protecting the rights and welfare of human research subjects; and
* promptly reporting to the IRB any unanticipated problems involving risks to research participants.

## 9.3 Provost and Executive Vice Chancellor for Academic Affairs

The Provost and Executive Vice Chancellor for Academic Affairs (Provost) is responsible for appointing members to serve on the IRB. Recommendations for appointees may be made by the Committee on Committees.

## 9.4 Vice Chancellor for Research and Innovation

The Vice Chancellor for Research and Innovation (Vice Chancellor) serves as the Chief Research Officer and reports to the Provost. The Office of the Vice Chancellor is responsible for overall administration and oversight of research activities at the University.

## 9.5 Director of Research Compliance

The Director of Research Compliance oversees the Office of Research Compliance (RSCP), a unit of the Office of the Vice Chancellor for Research and Innovation. The Director is responsible for assisting faculty, staff and students in complying with federal and state regulatory requirements pertaining to HSR, regardless of funding source, and with applicable University policies.

## 9.6 IRB Coordinator

The IRB Coordinator reports to the Director of Research Compliance and is responsible for:

* assisting researchers with the preparation and submission of research protocols;
* receiving and reviewing all protocols and requests for exemptions, to ensure there are no obvious errors or omissions;
* reviewing and approving, or distributing for review and approval by the IRB, all requests for exemptions;
* assigning protocols for Expedited Review and/or Full Committee Review, as appropriate to voting members of the IRB;
* obtaining additional information, clarifications, and/or expert advice as requested by reviewers;
* scheduling meetings and ensuring that official business is conducted only when a quorum of IRB voting members is present;
* preparing and maintaining documentation of IRB activities in accordance with federal policy;
* informing researchers of the outcome of protocol reviews including requests for additional information; clarifications; disapprovals; conditional approvals; and approvals;
* ensuring that all investigators and research staff on a protocol have completed the required [CITI](https://www.citiprogram.org/?pageID=668) training;
* reviewing requests for protocol modifications and/or continuations and distributing for Expedited Review or Full Committee Review as appropriate;
* sending annual reminders (or more often, as determined by the IRB) to the Principal Investigator of impending protocol expirations or reporting deadlines; and
* preparing additional reports and/or correspondence as requested by the Director of Research Compliance and/or IRB Chair.

## 9.7 Institutional Review Board (IRB)

The IRB functions as an independent standing committee whose members are appointed by the Provost. In accordance with University Policy, the IRB is responsible for:

* reviewing all HSR protocols, except those determined to be exempt, to ensure compliance with HHS requirements;
* documenting IRB activities in accordance with federal regulations and University policies; and providing advice and counsel to investigators engaged in HSR;
* assisting with the development of policies, procedures, information, and instructions for researchers who wish to conduct HSR; and
* reporting any unanticipated problems involving risks to research participants and others to the appropriate funding agency; and reporting to the appropriate University officers and appropriate funding agency(ies) any serious or continuing failure of investigators to comply with the requirements and determination of the IRB.

### 9.7.1 IRB Composition

In accordance with 45 CFR 46.107, the IRB must comprise at least five members with varying backgrounds to promote adequate review of research activities commonly conducted by the University. The Director of the University Health Services will serve as an *ex officio*, voting member. The Director of Research Compliance, or his/her designee, will serve as an *ex officio*, non-voting member.

The membership of the IRB must include:

* at least one member whose primary concerns are in a scientific area;
* at least one member whose primary concerns are in a non-scientific area; and
* at least one community member who is not otherwise affiliated with the University and who is not an immediate family member of a person who is affiliated with the University.

To reflect the diversity of research conducted at the University, the IRB will also include the following members:

* one graduate student;
* two faculty members each from the College of Education and Health Professions and Fulbright College of Arts and Sciences;
* one faculty member from each of the following: Walton College of Business; Bumpers College of Agricultural, Food and Life Sciences; College of Engineering; School of Architecture; the School of Law.

Every nondiscriminatory effort will be made to ensure that the IRB memberships includes both men and women. However, appointment to the IRB may not be made solely on the basis of sex.

A member may fulfill one or more of the requirements for the IRB (e.g. a community member who is also a scientist). However, the IRB must always include at least one member whose primary concerns are in scientific areas and one member whose primary concerns are in non-scientific areas. The unaffiliated community member represents the perspective of research participants when reviewing protocol submissions.

When the IRB reviews protocols that include one or more vulnerable categories of research subjects such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, the IRB must consider if the voting membership is sufficiently knowledgeable and experienced in working with these groups. The IRB may appoint one or more non-voting expert consultants to provide the necessary expertise to review these protocols. In accordance with 45 CFR 46.304, when the IRB reviews protocols involving prisoners, the composition of the IRB must include at least one voting member who is a prisoner or is a prisoner representative with appropriate background and experience to serve in that capacity. A majority of the Board, exclusive of the prisoner membership) cannot have any association with the prisoner(s) or representative(s), other than through membership on the IRB.

The Provost may appoint a member of the IRB who will serve as the expert on vulnerable categories.

### 9.7.2 IRB Chair

The Provost will designate one member of the IRB to serve as the Chair. The appointee must have at least one year of experience as a voting member of the IRB prior to assuming the duties and responsibilities of the Chair. In the event the Chair is unable to continue his/her term, the Provost will designate a replacement to serve as the Chair. In the event the Chair is temporarily unable to serve or is unable to attend one or more meetings of the IRB, the Chair shall appoint an Acting Chair. The Acting Chair must have at least one year of experience as an IRB member.

### 9.7.3 Expert Consultants

Per 45 CFR 46.107(f), the IRB may invite individuals with expertise in particular areas to assist in the review of protocols which require expertise beyond or in addition to that available from IRB members. These experts are not members of the IRB and may not vote on protocols. Expert consultants must disclose any potential conflicts of interest.

### 9.7.4 Alternates

 The University does not allow the use of alternate members.

### 9.7.5 IRB Roster

The Roster of current members of the IRB may be viewed on the [Provost’s website](https://provost.uark.edu/committees/irb.php).

### 9.7.6 IRB Member Terms

The graduate student, community member, and *ex officio* members will serve annual terms on the IRB. All other members are appointed for five-year terms, unless they are selected to fill a vacancy which occurs during the middle of a term. New terms begin in October to ensure that experienced IRB members are available through the summer term to review and approve protocols as needed.

Terms expire on a staggered basis to ensure that the voting membership always includes experienced members.

Membership on the IRB may be renewed for an unlimited number of consecutive five-year terms. The IRB Chair is expected to hold this position for at least one full term.

### 9.7.7 Conflicts of Interest

To adequately protect participants in HSR, all IRB members, expert consultants, and researchers are required to disclose any possible conflicts of interest or commitment in accordance with University policy 404.0: Conflict of Interest and Conflict of Commitment, Including Outside Activity.

When submitting a protocol for either Expedited Review or Full Committee Review, researchers must confirm that they have fulfilled the requirements of the University policy. If a conflict is disclosed, the IRB will not approve a protocol until the investigator has an approved conflict management plan.

### 9.7.8 Evaluation of the IRB

The Director of Research Compliance will periodically review and evaluate University IRB policies, membership, and procedures and provide recommendations to the Provost. Policies and procedures will be updated as needed (*e.g.* to reflect changes in federal policy).

### 9.7.9 Multi-Site Protocols: Cooperative Agreements for Reviews

Each institution or entity involved in HSR is responsible for safeguarding the rights and welfare of research participants. To avoid duplication of effort among participating institutions or entities, cooperative agreements may be used such that protocol review and approval is provided by the IRB of one of the institutions or entities involved in the effort. All such arrangements must be documented in writing and must be approved by all participating IRBs.

Effective January 20, 2020, single IRB review for multi-institutional studies not sponsored by the NIH will be required.

Multi-site studies funded by the NIH are required to use single IRB review effective January 25, 2018.

### 9.7.10 Federal-wide Assurance

The University of Arkansas IRB maintains an assurance (FWA #00001952) with the HHS Office for Human Research Protections (OHRP).

# 10. Framework for Due Process and Sanctions for Noncompliance

The IRB has the authority to suspend or terminate any research protocol that does not comply with federal regulations or University policies or that has been associated with serious harm to research participants. If the IRB determines that an incident of non-compliance exists, the IRB will report such incident to the appropriate institutional officials in a timely fashion, in accordance with OHRP reporting requirements.

The University of Arkansas process for addressing incidents of noncompliance is as follows:

## 10.1 Due Process

1. The Office of Research Compliance (RSCP) is made aware of a possible incident of noncompliance. Incidents may be reported to the Director, to the IRB Coordinator, or to any member of the IRB.

2. Within 24 hours of receipt of the initial report, RSCP will request information pertaining to the event from researchers. Once a request is made, researchers have five (5) business days to respond. Routine incidents of administrative noncompliance may be handled and corrected by the IRB Coordinator. If the alleged incident of noncompliance potentially places research subjects at **immediate risk**, the IRB Chair may order that all research activity be halted for up to 48 hours so that a preliminary assessment may be made.

3. Within five (5) business days of the researcher’s response to the request for information, a meeting is scheduled among an IRB noncompliance subcommittee, comprising the IRB Chair and two voting members, and the researchers. Researchers are invited but are not required to attend this meeting. The subcommittee may take the following actions:

1. Take no action, if the subcommittee finds that the report of noncompliance is unfounded.
2. Determine that an incident of noncompliance did occur and recommend appropriate corrective actions and/or sanctions.
3. Decide to collect additional information before taking further action.
4. Present its findings to the full IRB for further review.

4. If the subcommittee refers the review to the full IRB, within ten (10) business days of the subcommittee meeting, a meeting of the full IRB and researchers is scheduled. The full IRB may take the following actions:

1. Take no action, if the full committee finds that the report of noncompliance is unfounded.
2. Determine that an incident of noncompliance did occur and recommend appropriate corrective actions and/or sanctions.
3. Decide to collect additional information before taking further action.
4. The IRB decision is referred to the Provost.

5. If further action is required, a meeting is scheduled among the Provost, Vice Chancellor, Director of Research Compliance, the IRB Chair and the researchers. Following review and discussion, the Provost and/or Vice Chancellor may:

1. Take no action, if either the Provost and/or Vice Chancellor finds that the report of noncompliance is unfounded. **Note: if the IRB determines that an incident of non-compliance occurred that warranted a halt to the research, neither the Provost nor Vice Chancellor may overrule that determination and restart the research without the concurrence of the IRB.**
2. Determine that an incident of noncompliance did occur and recommend appropriate corrective actions and/or sanctions.

## 10.2 Sanctions for Noncompliance

The IRB or the noncompliance subcommittee provides recommendations for appropriate corrective actions and sanctions. Sanctions are implemented by the Provost and vary based on the nature and severity of the incident. Sanctions may include, but are not limited to:

* Removal of researcher(s) from the project under review;
* A letter of reprimand from the IRB;
* A letter of reprimand from the Provost;
* Additional reporting requirements;
* Special monitoring of future work, including random administrative audits;
* Probation and/or suspension, with or without pay;
* Salary reduction;
* Reduction in rank; and
* Termination of employment.

## 10.3 Reporting Significant Incidents of Noncompliance to OHRP

For significant incidents of noncompliance, the Director of Research Compliance will make an initial report to OHRP as soon as possible, but no later than 30 days from the time the IRB or the Office of Research Compliance is notified of the incident.

# 11. FDA-Specific Requirements

If a protocol involves the clinical investigation of a test article, such as a drug or medical device, the IRB must ensure that the protocol meets additional FDA regulatory requirements in addition to the protections discussed above.

## 11.1 Specific Data Safety and Monitoring (DSM) Plans

 A DSM plan must be reviewed by the IRB for:

* Phase I or Phase II clinical trials; and
* Protocols involving the study of FDA-approved drugs for which there has been a new safety warning issued or a change of labeling for drugs indicating increased risks.

## 11.2 University Reporting to the FDA: Unanticipated Problems or Incidents of Research Noncompliance

In accordance with 21 CFR 56.108(b), the Director of Research Compliance will report the following incidents to the FDA as soon as possible, but no later than 30 days from the time the IRB or the Office of Research Compliance is notified of the incident:

* Any unanticipated problems involving risks to human research subjects or others;
* Any incident of serious or continuing noncompliance with FDA regulations, University policy or IRB determinations; and
* Any IRB suspension or termination of approval.

## 11.3 Use of Investigational or Unlicensed Test Articles

If a research protocol involves an investigational new drug that has not yet been licensed for marketing in the United States, the IRB will verify receipt of an approved Investigational New Drug Application (INDA), unless the test article meets one of the exemption criteria described in 21 CFR 312.2(b).

If a protocol is intended to determine the safety and effectiveness of a medical device, the IRB will verify receipt of an approved Investigational Device Exemption (IDE), unless the device meets one of the exemption criteria described in 21 CFR 812.2.

## 11.4 Exempt Protocols

Per 21 CFR 56.104, the following categories of FDA-regulated research are exempt from IRB review:

1. Any investigation which began before 7/27/1981 and was subject to the requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before 7/27/1981;
2. Any investigation began before 7/27/1981 and which was not otherwise subject to the requirements for IRB review under FDA regulations before that date;
3. Emergency use of a test article, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the test article at the institution is subject to IRB review.
4. Taste and food quality evaluations and consumer acceptance activities, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the USDA.

## 11.5 Expedited Review

The IRB may choose to review the following categories of research using the expedited review process described above:

* Categories of research approved for expedited review by the FDA (see 63 Fed. Reg. 60353; November 9, 1998) and found by the IRB to involve no more than minimal risk; and
* Minor changes in previously approved research protocols.

## 11.6 Investigator Qualifications and Responsibilities

The IRB, in accordance with E6 Good Clinical Practice Guidance (ICH-GCP E6 [April 1996]), will confirm that:

* Investigators are qualified through education, training, and experience to conduct the research;
* Investigators are thoroughly familiar with the appropriate use of the test article;
* A qualified physician (or dentist, as appropriate), who is an investigator or sub-investigator, will be responsible for all trial-related medical (or dental) decisions; and
* Investigators will ensure that adequate medical care is provided to a subject for any adverse events related to the trial.

## 11.7 FDA Waiver of IRB Requirements

 The FDA may at its discretion waive any of the requirements under 21 CFR 56.

# 12. Protocol Closure

It is the responsibility of the investigator to let the IRB know when a protocol is complete or has been terminated for any reason. The investigator may close the protocol through the Streamlyne system. Protocols must be closed when:

* All research activities, including data analysis and reporting, are complete; or
* The investigator decides not to initiate the study; or
* The investigator plans to leave the University and intends to continue the research activities at another institution.

NOTE: If an investigator plans to leave the university and continue the research at a new institution in collaboration with researchers at the University of Arkansas, the investigator and his/her UA collaborators must submit a protocol modification to name the UA collaborator as the protocol Principal Investigator. IRB approval may be required at the investigator’s new institution.

# APPENDIX A: Definitions for this Policy

**The University of Arkansas utilizes the definitions from 45 CFR 46.102:**

(a) Certification means the official notification by the institution to the supporting Federal department or agency component, in accordance with the requirements of this policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

(b) Clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

(c) Department or agency head means the head of any Federal department or agency, for example, the Secretary of HHS, and any other officer or employee of any Federal department or agency to whom the authority provided by these regulations to the department or agency

head has been delegated.

(d) Federal department or agency refers to a federal department or agency (the department or agency itself rather than its bureaus, offices or divisions) that takes appropriate administrative action to make this policy applicable to the research involving human subjects it conducts, supports, or otherwise regulates (e.g., the U.S. Department of Health and Human Services, the U.S. Department of Defense, or the Central Intelligence Agency).

 (e)

(1) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

(2) Intervention 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.

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

(4) 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

(5) Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

(6) An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

 (7) Federal departments or agencies implementing this policy shall:

(i) Upon consultation with appropriate experts (including experts in data matching and re-identification), reexamine the meaning of ``identifiable private information,'' as defined in paragraph (e)(5) of this section, and ``identifiable biospecimen,'' as defined in paragraph (e)(6) of this section. This reexamination shall take place within 1 year and regularly thereafter (at least every 4 years). This process will be conducted by collaboration among the Federal departments and agencies implementing this policy. If appropriate and permitted by law, such Federal departments and agencies may alter the interpretation of these terms, including through the use of guidance.

(ii) Upon consultation with appropriate experts, assess whether there are analytic technologies or techniques that should be considered by investigators to generate ``identifiable private information,'' as defined in paragraph (e)(5) of this section, or an ``identifiable biospecimen,'' as defined in paragraph (e)(6) of this section. This assessment shall take place within 1 year and regularly thereafter (at least every 4 years). This process will be conducted by collaboration among the Federal departments and agencies implementing this policy. Any such technologies or techniques will be included on a list of technologies or techniques that produce identifiable private information or identifiable biospecimens. This list will be published in the Federal Register after notice and an opportunity for public comment. The Secretary, HHS, shall maintain the list on a publicly accessible Web site.

(f) Institution means any public or private entity, or department or agency (including federal, state, and other agencies).

(g) IRB means an institutional review board established in accord with and for the purposes expressed in this policy.

(h) IRB approval means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.

(i) Legally authorized representative means 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. If there is no applicable law addressing this issue, legally authorized representative means an

individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

(j) Minimal risk means that 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.

(k) Public health authority means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or entity acting under a grant of authority from or contract with such public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its

official mandate.

 (l) Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they

are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of

information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with

providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

(m) Written, or in writing, for purposes of this part, refers to writing on a tangible medium (e.g., paper) or in an electronic format.

**The University of Arkansas utilizes the definitions from 45 CFR 46.202:**

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

(b) Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means.

(c) Fetus means the product of conception from implantation until delivery.

(d) Neonate means a newborn.

(e) Nonviable neonate means a neonate after delivery that, although living, is not viable.

(f) 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 a pregnancy test are negative or until delivery.

(g) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(h) 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. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part.

**The University of Arkansas utilizes the definitions from 45 CFR 46.303:**

As used in this subpart:

(a) Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

(b) HHS means the Department of Health and Human Services.

(c) Prisoner means 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.

(d) Minimal risk is 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.

**The University of Arkansas utilizes the definitions from 45 CFR 46.402:**

As used in this subpart:

(a) 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.

(b) Assent means a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

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

(d) Parent means a child’s biological or adoptive parent.

(e) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

**Other Definitions**

(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. OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events. Jan. 15, 2007.

(b) Consent: Consent means legally effective and informed consent obtained from each subject or the subject’s legal representative. Consent shall be in writing unless the research involves no more than minimal risk and consent can be reasonably inferred, or waiver is otherwise proper under these policies and procedures. When the research involves minors, consent shall be obtained from a parent or legal guardian. Consent must be obtained under circumstances that offer the subject or his/her representative sufficient opportunity to consider whether or not the subject should participate. Consent shall not involve any exculpatory language through which the subject or representative is made to waive or appear to waive any legal rights, or to release the researcher or the university or its agents from liability for negligence or other wrongdoing.

(c) OHRP: Office for Human Research Protections, Department of Health and Human Services

(d) Protocol: The written report from the researcher, describing the proposed research activities, provided to the IRB from which compliance with these policies and procedures can be ascertained.

(e) Unanticipated problems involving risks to subjects or others: OHRP considers unanticipated problems, in general, to include 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. Jan. 15, 2007.

(f) Vulnerable Population: Any group of human subjects that is likely to be compromised in its ability to make decisions in the best interests of its members. This includes those persons who suffer from a mental disability such as a psychiatric disorder (*e.g.* organic and functional psychoses, neuroses, personality or behavioral disorders, senility, etc.) or developmental disorders (*e.g.* mental retardation); persons under the influence of or dependent on drugs or alcohol; those suffering from degenerative diseases affecting the brain; terminally ill patients; persons with severely disabling physical handicaps; prisoners; and some children. Pregnant women and fetuses are specifically included.

**FDA-Specific Definitions:**

**The University of Arkansas utilizes the definitions from 21 CFR 50.3 for protocols falling under FDA regulations:**

As used in this part:

(a) Act means the Federal Food, Drug, and Cosmetic Act, as amended ([secs. 201](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS201&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))--[902](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS902&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)), [52](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS952&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) Stat. 1040 et seq. as amended ([21 U.S.C. 321](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS321&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))--[392](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS392&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)))).

(b) Application for research or marketing permit includes:

(1) A color additive petition, described in Part 71.

(2) A food additive petition, described in Parts 171 and 571.

(3) Data and information about a substance submitted as part of the procedures for establishing that the substance is generally recognized as safe for use that results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in [§§ 170.30](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS170.30&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) and [570.30](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS570.30&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(4) Data and information about a food additive submitted as part of the procedures for food additives permitted to be used on an interim basis pending additional study, described in [§ 180.1](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS180.1&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(5) Data and information about a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) An investigational new drug application, described in Part 312 of this chapter.

(7) A new drug application, described in Part 314.

(8) Data and information about the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320.

(9) Data and information about an over-the-counter drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in Part 330.

(10) Data and information about a prescription drug for human use submitted as part of the procedures for classifying these drugs as generally recognized as safe and effective and not misbranded, described in this chapter.

(11) [Reserved]

(12) An application for a biologics license, described in part 601 of this chapter.

(13) Data and information about a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, described in Part 601.

(14) Data and information about an in vitro diagnostic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in Part 809.

(15) An Application for an Investigational Device Exemption, described in Part 812.

(16) Data and information about a medical device submitted as part of the procedures for classifying these devices, described in section 513.

(17) Data and information about a medical device submitted as part of the procedures for establishing, amending, or repealing a standard for these devices, described in section 514.

(18) An application for premarket approval of a medical device, described in section 515.

(19) A product development protocol for a medical device, described in section 515.

(20) Data and information about an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for these products, described in section 358 of the Public Health Service Act.

(21) Data and information about an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in [§ 1010.4](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS1010.4&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(22) Data and information about an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in [§ 1010.5](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS1010.5&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(23) Data and information about a clinical study of an infant formula when submitted as part of an infant formula notification under section 412(c) of the Federal Food, Drug, and Cosmetic Act.

(24) Data and information submitted in a petition for a nutrient content claim, described in [§ 101.69](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS101.69&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter, or for a health claim, described in [§ 101.70](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS101.70&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter.

(25) Data and information from investigations involving children submitted in a new dietary ingredient notification, described in [§ 190.6](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS190.6&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter.

(c) Clinical investigation means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is 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. The term does not include experiments that are subject to the provisions of Part 58 of this chapter, regarding nonclinical laboratory studies.

(d) Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, 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.

(e) Sponsor means a person who initiates a clinical investigation, but who 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., corporation or agency) that uses one or more of its own employees to conduct a clinical investigation it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(f) 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., corporation or agency.

(g) Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

(h) Institution means any public or private entity or agency (including Federal, State, and other agencies). The word facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

(i) Institutional review board (IRB) means any board, committee, or other group formally designated by an institution to review biomedical research involving humans as subjects, to approve the initiation of and conduct periodic review of such research. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the act.

(j) Test article means any drug (including a 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 and 354–360F of the Public Health Service Act ([42 U.S.C. 262](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=42USCAS262&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) and [263b](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=42USCAS263B&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))–[263n](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=42USCAS263N&originatingDoc=N05936AE08CA511D9A785E455AAD0CC92&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))).

(k) Minimal risk means that 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.

(l) Legally authorized representative means 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.

(m) Family member means any one of the following legally competent persons: Spouse; 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.

(n) Assent means a child’s affirmative agreement to participate in a clinical investigation. Mere failure to object may not, absent affirmative agreement, be construed as assent.

(o) 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.

(p) Parent means a child’s biological or adoptive parent.

(q) Ward means 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.

(r) Permission means the agreement of parent(s) or guardian to the participation of their child or ward in a clinical investigation. Permission must be obtained in compliance with subpart B of this part and must include the elements of informed consent described in [§ 50.25](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS50.25&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(s) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. For purposes of subpart D of this part, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research.

**The University of Arkansas utilizes the definitions from 21 CFR 56.102 for protocols falling under FDA regulations:**

As used in this part:

(a) Act means the Federal Food, Drug, and Cosmetic Act, as amended ([secs. 201](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS201&originatingDoc=N6D9FAB206FC311DEA2E2CF2F08053657&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))–[902](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS902&originatingDoc=N6D9FAB206FC311DEA2E2CF2F08053657&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)), [52](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS952&originatingDoc=N6D9FAB206FC311DEA2E2CF2F08053657&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) Stat. 1040 et seq., as amended ([21 U.S.C. 321](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS321&originatingDoc=N6D9FAB206FC311DEA2E2CF2F08053657&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation))–[392](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000546&cite=21USCAS392&originatingDoc=N6D9FAB206FC311DEA2E2CF2F08053657&refType=LQ&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)))).

(b) Application for research or marketing permit includes:

(1) A color additive petition, described in Part 71.

(2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in [§ 170.35](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS170.35&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(3) A food additive petition, described in Part 171.

(4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in [§ 180.1](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS180.1&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) An investigational new drug application, described in Part 312 of this chapter.

(7) A new drug application, described in Part 314.

(8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in Part 320.

(9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in Part 330.

(10) An application for a biologics license, described in part 601 of this chapter.

(11) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, as described in part 601 of this chapter.

(12) An Application for an Investigational Device Exemption, described in part 812.

(13) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in Part 860.

(14) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealing a standard for such device, described in Part 861.

(15) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(16) A product development protocol for a medical device for human use, described in section 515 of the act.

(17) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(18) Data and information regarding an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in [§ 1010.4](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS1010.4&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(19) Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in [§ 1010.5](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS1010.5&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)).

(20) Data and information regarding an electronic product submitted as part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in Subpart D of Part 1003.

(21) Data and information about a clinical study of an infant formula when submitted as part of an infant formula notification under section 412(c) of the Federal Food, Drug, and Cosmetic Act.

(22) Data and information submitted in a petition for a nutrient content claim, described in [§ 101.69](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS101.69&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter, and for a health claim, described in [§ 101.70](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS101.70&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter.

(23) Data and information from investigations involving children submitted in a new dietary ingredient notification, described in [§ 190.6](http://www.westlaw.com/Link/Document/FullText?findType=L&pubNum=1000547&cite=21CFRS190.6&originationContext=document&vr=3.0&rs=cblt1.0&transitionType=DocumentItem&contextData=(sc.UserEnteredCitation)) of this chapter.

(c) Clinical investigation 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 Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that must meet the provisions of Part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part.

(d) Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient.

(e) Institution means any public or private entity or agency (including Federal, State, and other agencies). The term facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

(f) Institutional Review Board (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the act.

(g) Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, 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.

(h) Minimal risk means that 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.

(i) 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.

(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.

(k) 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.

(l) IRB approval means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.