3.1 Human Subjects Research Determination

The responsibility for an initial determination as to whether an activity constitutes human subjects research rests with the PI. The PI should make this determination based on the definitions of "human subject" and "research." The Institution holds PIs responsible for the correct determination. PIs are urged to request a confirmation that an activity does not constitute human subjects research from the OHRP. If the PI is unclear as to the research determination, contact the Office of Research Integrity and Compliance.

Determinations as to whether an activity constitutes human subjects research are made according to the regulatory definitions. Determinations regarding activities that are clearly or clearly not human subjects research, based on definitions, may be made by the OHRP Director. Determinations regarding activities that are more complex will be referred to the IRB Chair, who may make the determination or refer the matter to the full IRB.

Documentation of all determinations made through the OHRP will be recorded and maintained in the OHRP. Formal submissions will be responded to in writing, and a determination letter/email will be kept on file in the electronic system.

New Common Rule Updates:

Regulatory guidance for activities deemed not to be research:

- Scholarly and journalistic activities
- Government functions with separately mandated protections

Benign Behavioral Intervention: Interactions that are brief harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing

Clinical Trial: Research study in which human subjects are prospectively assigned to interventions to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Human subject: a living individual about whom an investigator conducting research obtains

- Information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens;
- Uses, studies, analyzes or generates identifiable private information

Interaction: communication or interpersonal contact

Intervention: physical procedures/environmental manipulations by which information or biospecimen are gathered
3.2 Exempt Studies

All research using human subjects must be approved by the Institution. Certain categories of research (i.e., "exempt research") do not require convened IRB review and approval. Exempt research is subject to institutional review and must be determined and approved by the IRB Chair or his/her designee. To qualify as exempt, the research must be not greater than minimal risk (Only Minimal Risk OMR) and must be in one of the exemption categories.

Minimal risk is defined by the federal regulations (45 CFR 46) as 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.

3.2.1 New Common Rule

- **Subpart B:**
  Studies Involving Pregnant Women, Fetuses & Neonates are Eligible for Exempt Under All 8 Categories

- **Subpart C:**
  Exemptions Do Not Apply to Research Involving Prisoners Except "for Research Aimed at Involving a Broader Subject Population that Only Incidentally Includes Prisoners"

- **Subpart D:**
  Children are allowed in categories 1,4,5,6,7 & 8; Limitations & Exclusion of Children in Category 2 & 3

3.2.2 Limitations on Exemptions

3.2.2.1 Children as Research Subjects in Exempt Studies

Exemption for research involving survey or interview procedures does not apply to research in children. Research involving observations of public behavior in children when the PI does not interact with the children being observed is considered exempt.

3.2.2.2 Prisoners as Research Subjects in Exempt Studies

Exemption for research does not apply. IRB review is required.

3.2.2 Categories of Exempt Research

Research activities not regulated by the FDA in which the only involvement of human subjects will be one or more of the following categories are exempt from IRB review, but require institutional review (note the exceptions above):

1. Research conducted in established or commonly (standard practice) accepted educational settings, involving normal educational practices, such as:
   a. Research on regular and special education instructional strategies; or
b. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless:
   a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
   b. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, or reputation.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
   a. The human subjects are elected or appointed public officials or candidates for public office; or
   b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and after that.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the PI in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

**NOTE:** To be eligible for this exemption category, all materials have to exist at the time the research is proposed.

5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:
   a. Public benefit or service program;
   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.
   e. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act).
   f. The research demonstration project must be conducted according to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects', and the exemption must be invoked only with authorization or concurrence by the funding agency.
6. Taste and food quality evaluation and consumer acceptance studies:
   a. If wholesome foods without additives are consumed; or
   b. 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

3.2.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of IRB review:

1. Emergency use of a test article provided that such emergency use is reported to the IRB within five working days. Any subsequent use of the test article at the Institution is subject to IRB review. [21 CFR 56.104(c)]

2. Taste and food quality evaluations and consumer acceptance studies, 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 Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR 56.104(d)]

3.2.6 Clarification of Exemption Category Four (4) Review

Research studies involving the collection of data from medical records may qualify as exempt from review under category four, provided that the following criteria are met:

1. The data must exist at the time of the exemption application. Studies wishing to collect data from the medical records of patients who have not yet been seen clinically would not qualify for exemption.

2. The data must be recorded without codes or links to patient identifiers (i.e., the medical record number (MRN)). For example, researchers often obtain a list of MRNs from patients with a specific condition being studied that they then use to locate medical records for the purposes of data collection. As long as no code or link is assigned to the patient that would allow linkage of the collected data and the specific medical record, this type of research may qualify for exemption. However, researchers wishing to assign such a link to enable revisiting of the medical record would need to apply for expedited approval. A HIPAA application should be submitted for both review types (exempt and expedited), and a consent form waiver will need to be submitted for medical records research not qualifying as exempt category four.

3.3 Expedited Review

An IRB may use the expedited review procedure to review either or both of the following:

1. Some, or all, of the research appearing on the list of categories of research eligible for
expedited review and found by the reviewer(s) to involve no more than minimal risk.

2. Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

**New Common Rule:**

- No continuing review of expedited research unless the IRB has a reason to require it and can justify that reason.
- No continuing review for projects conducting data analysis only.
- Expedited categories of IRB review will be annually evaluated by the HHS Office for Human Research Protections.

### 3.3.1 Categories of Research Eligible for Expedited Review

The activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. The categories in this list apply regardless of the age of the subjects, except as noted.

The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The expedited review procedure may not be used for governmental classified research involving human subjects. The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review – expedited or convened board – utilized by the IRB.

**NOTE:** Research categories one (1) through seven (7) pertain to both initial and continuing IRB review.

1. Clinical studies of drugs and medical devices, only when condition (a) or (b) is met:
   a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required.

**NOTE:** The WVU IRB has determined that all drug studies must be reviewed by a convened, full board.

   b. Research on medical devices for which:
      i. An investigational device exemption application (21 CFR 812) is not required; or
      ii. The medical device is cleared/approved for marketing, and the device is being used following its cleared/approved labeling

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550ml in eight weeks and collection may not occur more
frequently than two times per week; or

b. From other adults and children¹, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3ml per kilogram in 8 weeks, and collection may not occur more than two times per week.

   i. Children are defined in the DHHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. [45 CFR 46.402(a)]
3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include the following:
   a. Hair and nail clippings in a non-disfiguring manner
   b. Deciduous or permanent teeth at the time of exfoliation or if routine patient care indicates a need for extraction
   c. Excreta and external secretions, including sweat
   d. Uncannulated saliva, collected either in an unstimulated fashion or stimulated by chewing gum base, wax, or applying a dilute citric solution to the tongue
   e. Placenta removed at delivery
   f. Amniotic fluid obtained at the time of rupture of the membrane before, or during labor
   g. Supra- and sublingual dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth, and the process is accomplished following accepted prophylactic techniques
   h. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings
   i. Sputum collected after saline mist nebulization

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. Examples include the following:
   a. physical sensors that are applied either to the surface of the body or at a distance and do not involve the input of significant amounts of energy into the subject or an invasion of the subject's privacy
   b. weighing or testing sensory acuity
   c. magnetic resonance imaging
   d. electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electoretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography
   e. moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual

**NOTE:** Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.

5. Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for non-research purposes (such as medical treatment or diagnosis).
NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing a survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

NOTE: Some research in this category (7) may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.

8. Continuing review of research previously approved by the convened IRB as follows:
   a. The research is permanently closed to the enrollment of new subjects for longer than a year;
   b. All subjects have completed all research-related interventions; and
      i. The research remains active only for long-term follow-up; or
      ii. Where no subjects have been enrolled and no additional risks have been identified; or
      iii. Where the remaining research activities are limited to data analysis.

NOTE: Category (8) identifies three situations in which research that is greater than minimal risk, and has been initially reviewed by a convened IRB, may undergo subsequent continuing review by the expedited review procedure.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8) (a), (b), or (c) are satisfied for that site. However, for category 8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the PI nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories two (2) through eight (8) do not apply, but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.
   a. The determination that "...no additional risks have been identified" does not need to be made by the convened IRB.
3.4 Reliance Reviews

3.4.1 WVU is NOT the IRB of Record

3.4.1.1 External IRB Review - Central Institutional Review Board (CIRB)

Central IRB protocol registrations are typically externally funded. These protocols are reviewed by an external CIRBs for which WVU has a master reliance agreement in place.

Depending on which of the CIRBs serve as the IRB of record, the Principal PI (submitting party) or managing party will be billed for an Administrative Review conducted by the WVU Office of Research Integrity and Compliance (OHRP).

Information regarding CIRBs that are approved for use can be found on the WVU OHRP website.

New Common Rule:

External IRB Review – Multi-site Research Single IRB (sIRB)

- Single IRB review will be required for all federally funded, cooperative research studies effective January 2020 (NIH already requires single IRB review)
- Reviewing IRB must be identified by the funding department or agency or proposed by the lead institution

Refer to the WVU OHRP website for guidance on sIRB.

3.4.2.1 Submission for Initial Review (WVU Relying Site)

The local (WVU) PI must submit items to the local IRB for review when WVU is relying on other institutions as the IRB of Record. Items to be submitted during an initial submission include:

1. Approved Protocol
   a. Sponsor (if applicable)
   b. Researcher Initiated
2. PI Brochure
3. Device Manual
4. Informed Consent Document(s)
   a. Must use the WVU specific template wording
5. IRB of Record Approval Letter

3.4.2.2 Submission for Continuing Review (WVU Relying Site)

Continuing reviews are not required when WVU is NOT the IRB of Record.

3.4.3 Submission of Study-wide Amendments

Amendments are not required when WVU is NOT the IRB of Record.
3.4.4 Reporting Events

Should any potential unanticipated problems, serious or continuing non-compliance, or support suspensions or terminations occur, WVU OHRP SOP and guidance for event reporting are required to be followed.