Organizational Policy		
Current Status: *Active*		Policy Number: RI-20
CATAWBA VALLEY HEALTH SYSTEM	Origination:	01/23/2008
	Last Reviewed:	01/16/2023
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	Responsible for Content:	Research & EBP
	Document Area:	Patient Rights
	Applicability:	☑ CVMC ☑ CVMG
	Exclusions:	☑ No Exclusions

INSTITUTIONAL REVIEW BOARD

I. POLICY

Catawba Valley Health System (CVHS) respects its patients, their rights, and the confidentiality of their medical information in human subject research. The Catawba Valley Med Center Institutional Review Board (IRB) reviews research and clinical investigations/trials that are proposed to be conducted at CVHS involving subjects who are currently, have been, or could by study design become patients of CVHS s and/or subjects who are currently or have been CVHS employees. The IRB acts in accordance with the ethical principles of respect for persons, beneficence, and justice in its review and monitoring of human subject research.

II. FUNCTIONS

The IRB complies with the Code of Federal Regulations (CFR) as outlined in 45 CFR 46 and 21 CFR 50 & 56 in review and monitoring of proposed research and clinical investigations/trials:

A. Approves, modifies, or disapproves proposed research covered by this policy and notifies investigators of its decision(s) in writing.
B. Requires documentation of informed consent, waives documentation of informed consent, or waives securing informed consent.
C. Conducts continuing review of approved research at intervals appropriate to the degree of risk, but not less than once per year.
D. Requires that any change(s) to previously approved research be submitted by the investigator to the IRB with the stipulation that changes cannot be implemented prior to review, approval and written notification of approval of the changes.
E. Requires unanticipated problems and unanticipated adverse events with untoward risk to the subject be reported by the investigator within 24 hours to the IRB Chair or his/her designee by phone or email and within seven (7) days in writing.
F. Exercises the right to suspend or terminate approved research that is not being conducted in accordance with IRB requirements.

III. STRUCTURE

A. Board Composition

Designed to be diverse in membership and fair in execution of its duties, the IRB has a minimum of five members with varying backgrounds to promote thorough review of research commonly conducted at CVHS.

1. Membership to include:
    a. At least one member whose primary concerns are in scientific areas.
    b. At least one nonscientific member.
    c. At least one member who is not otherwise affiliated with CVHS.
    d. And not to consist entirely of men or entirely of women.
2. The IRB may at its discretion invite individuals with competence in specialized areas to assist in the review of research when expertise beyond that of its members is required.
3. Alternate members may be appointed to serve in the absence of appointed members with similar expertise. The alternate serves in all capacities of IRB membership during the absence of the appointed member. An alternate's vote will not count toward the quorum if the appointed member they represent is also present.

B. Convened Meetings
1. Meetings are scheduled bi-annually.
2. Additional meetings are scheduled at the discretion of the IRB Chair or Vice-Chair.
3. Teleconferences are acceptable provided each participating IRB member has received all pertinent material prior to the call and can actively and equally participate in the discussion. Satisfaction of these conditions will be documented in the meeting minutes.
4. In the absence of agenda items that require a vote of the IRB, scheduled meetings may be cancelled, but at least one meeting will be held annually.
5. Investigators may attend meetings upon request of the IRB Chair or Vice-Chair. However, they are dismissed prior to the IRB acting on their research, which is under review.

C. Research Review
1. For full guidelines outlining IRB review of research, please review section §46.109 of the 2018 Common Rule (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.109).
2. Except when an expedited review procedure is used, the IRB reviews proposed research at convened meetings at which a majority of IRB members are present, including at least one nonscientific member, i.e., a quorum. In order for research to be approved, it must receive a majority vote of this quorum. Should the quorum fail during a meeting (e.g., through recusal of members with conflicting interests, early departures, etc.), the IRB cannot take further action, i.e. vote, unless the quorum is restored.
3. No member participates in initial or continuing review of research in which the member has a conflicting interest, except to provide information as requested by the IRB.

D. Administrative Relationships
1. The IRB reports to the organization's Patient Rights Council (PRC) any unanticipated problems and unanticipated adverse events (RI-20-V.E) of which investigators inform the IRB.
2. Information reports to the PRC, provided upon request, include, but are not limited to, number of active research studies and board member education compliance.

IV. ROLES & RESPONSIBILITIES

A. Chair
   1. Appointment by the IRB Head Official.
   2. Duties:
      a. Presides at meetings of the IRB;
      b. Implements IRB policies and procedures;
      c. Provides the agenda and research proposal documents to IRB members in advance of scheduled meetings;
      d. Ensures that appropriate documentation of IRB proceedings and business occurs;
      e. Appoints subcommittees as deemed appropriate;
      f. Represents the IRB to investigators and serves as their direct IRB contact.

B. Vice Chair
   1. Appointment by the IRB Head Official.
   2. Duties:
      a. Presides at meetings of the IRB at the request of the Chair;

C. IRB Members
   1. Appointed by the IRB Chair and may serve unlimited reappointments
   2. Duties:
      a. Review research proposal documents in advance of IRB meetings;
      b. Vote to approve, disapprove, or modify proposed research;
      c. Comply with competence requirements;
      d. Attend at least 50% of convened meetings in any given year – failure to do so may serve as grounds for dismissal from the IRB.

D. Protecting Human Research Participants (PHRP) Education
   1. Members are required to complete basic education in human subject protection prior to beginning service on the IRB.
   2. Member PHRP completion certificates are held in the permanent IRB records.
   3. On a continuing basis, IRB members complete education to maintain and extend their competence.
   4. PHRP education may be accomplished by participating in any of the following:
      a. National Institutes of Health (NIH) Office of Extramural Research Protecting Human Research Participants;
      b. Department of Health and Human Services (HHS) Office of Human Research Protections (OHRP) Human Subject Assurance Training;
      c. Collaborative Institutional Training Initiative (CITI) courses;
      d. Education equivalent to or exceeding a-c is required for initial PHRP training;
      e. Continued PHRP proficiency may be fulfilled by participating in OHRP online tutorials/webinars, conferences, and/or in-service education opportunities.

E. Orientation
   1. The Chair or his/her designee conducts member orientation.
   2. Members receive and review IRB policy and procedures, resources, and secure web portal instruction.
   3. Prior to assuming duties, members must provide evidence of completed PHRP education.

F. Liaison
   1. CVHS Head Official designates the Liaison.
   2. Duties:
      a. Records minutes of IRB meetings as described in RI-20-VI.B.;
      b. Informs investigators of progress reports due dates prior to the due dates;
      c. Reserves meeting dates and locations;
      d. Maintains the permanent files of the IRB.

V. PROCEDURES

A. Research Review
   1. Application forms are available at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx. Certain supporting documents are required to constitute a complete research application, e.g., PHRP completion certificate. Initially, an investigator submits his/her application to the Administrator for Research and Evidence-Based Practice. The Administrator communicates with the investigator as needed to ensure the application is complete. The investigator then submits his/her signed application to the IRB Chair or Vice Chair electronically.
   2. In approving research, the IRB determines the following criteria are satisfied (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.111):
      a. Risks to subjects are minimized:
         (i) By using procedures which are consistent with sound research design, and which do not unnecessarily expose subjects to risk, and
         (ii) Whenever appropriate, procedures already being performed on the subjects for diagnostic or treatment purposes are utilized;
      b. Risks to subjects are reasonable in relation to anticipated benefits, if any;
      c. Selection of subjects is equitable;
      d. Informed consent is sought from each prospective subject or his/her legally authorized representative and the consent documented unless waiver of documentation or waiver of consent applies;
      e. Adequate provisions are made to protect the privacy of subjects and to maintain confidentiality of the data; and
      f. Additional safeguards are included in the research to protect the rights of subjects likely to be vulnerable to coercion or undue influence, e.g., children, prisoners, pregnant women, mentally disabled persons, etc.; when such subjects are being recruited for the research in accordance with applicable regulations.
   3. HHS Decision Charts (https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts-2018/index.html) are utilized by the IRB Chair and/or his/her designee to determine whether proposed research qualifies as exempt from review, qualifies for expedited review, or requires full board review. IRB members utilize the decision charts in their review of research applications.

B. Review Categories
   1. Exempt from Review

a. For full guidelines outlining Exempt Research, please review section §46.104 of the 2018 Common Rule (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.104).
b. Research which presents no foreseeable risks to subjects may qualify for exemption from IRB review. To adequately protect the rights of human subjects, the IRB shall make determinations of exemption for proposed research.
c. The investigator is informed in writing when his/her proposed research qualifies as exempt from IRB review noting that exemption does not necessarily negate obtaining informed consent from subjects.

2. Expedited Review
   a. The IRB uses expedited procedures to review:
      (i) Applicable research (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.110) involving no more than minimal risk, and
      (ii) Minor changes in previously approved research during the period for which approval is authorized.
   b. Expedited review is conducted by the IRB Chair or by his/her designee.
   c. Expedited reviewers exercise the authorities of the IRB except that they may not disapprove the research under review.
   d. Documentation for initial and continuing reviews conducted under an expedited review procedure includes the specific category justifying the expedited review in the written investigator communication.
   e. The Chair ensures all IRB members are advised of research proposals approved via expedited review.
3. Full Board Review
   a. Proposed research, not qualifying for expedited review, is reviewed at a convened meeting of a quorum of the IRB.
   b. The IRB designates the level of risk posed to human subjects as required by federal regulations. Research deemed to be of minimal risk is reviewed annually. Research deemed to constitute more than minimal risk to subjects is reviewed every six months at a minimum or more frequently at the discretion of the IRB. See RI-20-VIII. for risk definitions.

C. Types of Review
1. Initial Review
   a. Commences upon receipt of a complete research application, to include:
      (i) full research protocol;
      (ii) supporting documents, e.g., instruments, data collection tools, external IRB approval letter, etc. as applicable
      (iii) proposed informed consent document or consent waiver request;
      (iv) recruitment materials, including advertisements intended to be seen or heard by potential subjects;
      (v) PHRP completion certificate(s); and
      (vi) evidence of current HIPAA compliance.
   b. The research may be reviewed under expedited or full board procedures.

2. Continuing Review
    a. The IRB conducts continuing review of approved research at least annually, which provides an opportunity to reassess the totality of the study and assure that risks to subjects are being minimized and are still reasonable in relation to anticipated benefits, if any, to the subjects. More frequent continuing review occurs when dictated by the degree of risk associated with the research.
    b. When conducting continuing review, the IRB begins with the working assumption that the research, as previously approved, satisfies the criteria for approval [RI-20-V.A.2.]. The IRB then focuses on whether any new information, provided by the investigator, alters prior determinations, particularly with respect to its prior evaluation of the potential benefits and/or risks to the subjects, and assesses whether any new information necessitates revision of the study protocol and/or the informed consent document.
    c. Continuing IRB review is preceded by receipt of a written progress report from the investigator to include, but not limited to, the number of subjects enrolled, number of withdrawn subjects and reasons for withdrawal, results to date, current risk-benefit assessment, and any new pertinent information since the last IRB review. A copy of the consent document, currently in use by the investigator, must be appended to the progress report unless consent has been waived. The progress report form is available at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx
3. Cooperative Review
    a. Cooperative research projects covered by this policy are those that involve more than one institution or organization. When CVHS participates in cooperative research, the IRB may:
        (i) Enter into a joint review arrangement with another institution; or
        (ii) Rely upon the review of another qualified IRB.
    b. When relying on another IRB, the IRB ensures that the reviewing IRB's Federal Wide Assurance (FWA) is active. A formal IRB Authorization Agreement will be executed between the two entities, and the signed document retained in the permanent files of the IRB.
    c. Regardless of the IRB's arrangement decision, it recognizes it is still responsible for safeguarding the rights and welfare of CVHS human subjects.
    d. When making cooperative research decisions, the IRB reviews a copy of the approved research application to include, but not limited to, the full protocol, informed consent document(s), and external IRB approval letter.
4. Humanitarian Device Exemption (HDE) Protocol Review
    a. Physicians desiring to utilize a Humanitarian Use Device (HUD) at CVHS must submit the following evidence to the IRB:
        (i) FDA approval letter(s);
        (ii) Treatment protocol;
        (iii) Patient materials to be provided to patients being considered for the treatment; and
        (iv) Any other pertinent documents

b. Physicians must inform the IRB of any intention to use a HUD outside of its FDA-approved indication. Obtaining informed consent will be required by the IRB in these cases of HUD use.

c. The IRB utilizes the Food and Drug Administration (FDA) guidance document for HDE to clarify questions that arise in the review of HDE protocols.

D. Protocol Changes

1. Review of Protocol Changes

a. The investigator is responsible for submitting any amendment(s) to his/her approved study prior to implementing the desired change(s) using a standard form (https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx).

b. Protocol changes are to be incorporated into the previously approved protocol. The investigator then retitles the revised protocol to include the version number, e.g., first instance of requested changes – Title, Version 2. The same procedure is used for informed consent form (ICF) revisions. The investigator submits the revised documents to the IRB. Once approved, the revised protocol and ICF versions supersede the previous version(s).

c. The IRB evaluates protocol changes submitted by the investigator using the same review criteria required at initial review. Minor changes may qualify for expedited review [RI-20-V.B.2 (ii)].

d. The IRB will evaluate if the protocol change(s) alters the risk to human subjects involved in the research. If the amendment increases the risk, the IRB will alter the continuing review period accordingly.

E. Reporting of Unanticipated Adverse Events and Unanticipated Problems

1. Adverse Events

Although there is no common definition of adverse event across government and non-government entities, the following broad definition is used by the IRB.

a. Broadly defined, an adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, (e.g., 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.

b. Adverse events encompass both physical and psychological harms.

c. They occur most commonly in the context of biomedical and clinical research but can occur in the context of social and behavioral research.

d. In the context of multicenter trials, adverse events can be categorized as either internal adverse events or external adverse events

(i) Internal adverse events: those experienced by subjects enrolled by the investigator at CVHS.

(ii) External adverse events: those experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial.

2. Unanticipated Problems

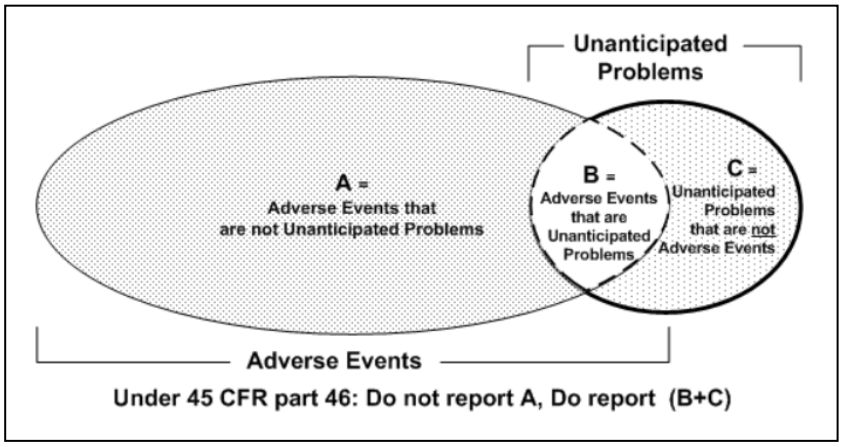
Any incident, experience, or outcome meeting all the following criteria is defined as an unanticipated problem:

a. Unexpected (in terms of nature, severity, or frequency) given

(i) the research procedures that are described in the previously approved study protocol and informed consent document; and
(ii) the characteristics of the subject population being studied;

b. Related or possibly related to a subject's participation in the research; and
c. Suggesting that the study places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) related to the research than was previously known or recognized.

3. How to Determine if an Adverse Event represents an Unanticipated Problem
   a. Ask the following three questions:
      (i) Is the adverse event unexpected?
      (ii) Is the adverse event related or possibly related to participation in the research?
      (iii) Does the adverse event suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized?
   b. If the answer to **all** three questions is yes, then the adverse event is an unanticipated problem.
4. Reporting of Unanticipated Problems and Unanticipated Adverse Events
   Unanticipated problems involving risks to subjects or others and adverse events that are unanticipated must be reported by the investigator as follows:
   a. The investigator is responsible for reporting unanticipated problems and unanticipated adverse events within 24 hours to the IRB Chair or his/her designee by phone or email and in writing to the IRB within in seven days. When appropriate, the investigator reports the unanticipated problem or unanticipated adverse event to HHS.
   b. Investigator reports of unanticipated problems and unanticipated adverse events are reported by the IRB to the CVHS patient Rights Council. The IRB reviews reports of unanticipated problems and unanticipated adverse events in accordance with guidance provided by federal agencies.
   Example of an unanticipated problem not classified as an adverse event that is reportable to the IRB: An investigator conducting behavioral research collects individually identifiable sensitive information about illicit drug use and other illegal behaviors by surveying college students. The data are stored on a laptop computer without encryption, and the laptop is stolen from the investigator's car. This is an unanticipated problem that must be reported because the incident was (1) unexpected, i.e., the investigator did not anticipate the theft; (2) related to participation in the research; and (3) places the subjects at a greater risk of psychological and social harm, than was previously known or recognized, from this breach in confidentiality of the study data.
   c. The relationship between adverse events and unanticipated problems is shown in the following diagram. Investigators must report 'Z' (unanticipated problems) and 'Y' (unanticipated adverse events); however, they do not report 'X' (anticipated adverse events) to the IRB.



F. Informed Consent

A hallmark of ethical human subject research is its voluntary nature. In most instances, voluntary participation of subjects is obtained by securing their informed consent. The IRB reviews proposed informed consent forms (ICF) per the following guidelines:

1. General
    a. Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative.
    b. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.
    c. The information that is given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative.
    d. The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
    e. Except for broad consent obtained in accordance with paragraph (RI-20-V.F.4) of this section: (i) Informed consent must begin with a concise focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. (ii) Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective

subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

f. Consent does not include any exculpatory language, e.g., subjects cannot be forced to waive/give up legal rights or be given the impression that they are being asked to do so.

2. Basic Elements
    a. A statement that the activity involves research.
    b. An explanation of the purposes of the research.
    c. The expected duration of the subject's participation.
    d. A description of the procedures to be followed.
    e. Identification of the procedures which are experimental.
    f. A description of any reasonably foreseeable risks or discomforts to the subject.
    g. A description of any benefits to the subject or others which may reasonably be expected from the research.
    h. Disclosure of appropriate alternative procedures or courses of treatments, if any, that might be advantageous to the subject.
    i. A statement describing the extent to which confidentiality of records identifying the subject will be maintained.
    j. For research involving more than minimal risk, an explanation as to whether any compensation or medical treatment is available if injury occurs and, if so, what it may consist of, or where further information may be obtained.
    k. Who to contact for pertinent questions about the research, human subjects' rights, and research-related injury.
    l. This human rights statement is to be included: A statement describing participation is voluntary and refusal to participate will not result in penalty or loss of benefits to which the subject is otherwise entitled and that the subject may discontinue participation at any time without penalty or loss of benefits to which he/she is otherwise entitled.
    m. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens: (i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent form the subject or the legally authorized representative, if this might be a possibility; or (ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
3. Additional Elements (as appropriate)
    a. A statement that the particular treatment/procedure may involve risks to the subject, or to an embryo or fetus, if the subject is pregnant or may become pregnant, that are currently unforeseeable;
    b. Anticipated circumstances under which a subject's participation may be terminated by the investigator without regard to the subject's consent;
    c. Any additional costs to the subject that may result from participation;

d. The consequences of the subject's decision to withdraw from the research and the procedures of orderly termination of participation by the subject;
e. A statement that significant new findings developed during the course of the research, which may be related to the subject's willingness to continue participation, will be provided to the subject;
f. The approximate number of subjects involved in the study;
g. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
h. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
i. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

4. Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable specimens.
Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements in paragraphs (RI-20-V.F.2) and (RI-20-V.F.3) of this section. If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative:
    a. The information required in paragraphs (RI-20-V.F.2.b), (RI-20-V.F.2.c), (RI-20-V.F.2.e), and (RI-20-V.F.2.h) and, when appropriate, (RI-20-V.F.3.g) and (RI-20-V-F.3.i) of this section;
    b. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;
    c. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;
    d. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite);

e. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

f. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and

g. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

5.Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials (see section §46.116 (e) of the 2018 Common Rule at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116)

6.General waiver or alteration of consent

a. *Waiver.* An IRB may waive the requirement to obtain informed consent for research under paragraphs (RI-20-V.F.1) through (RI-20-V.F.3) of this section, provided the IRB satisfies the requirements of paragraph (RI-20-V.F.6.c) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (RI-20-V.F.4) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

b. *Alteration.* An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in paragraphs (RI-20-V.F.2) and (RI-20.V.F.3) of this section provided the IRB satisfies the requirements of paragraph (RI-20-V.F.6.c) of this section. An IRB may not omit or alter any of the requirements described in paragraph (RI-20-V.F.1) of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (RI-20-V.F.4) of this section.

c. *Requirements for waiver and alteration.* In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:

(i) The research involves no more than minimal risk to the subjects;
(ii) The research could not practicably be carried out without the requested waiver or

alteration;
(iii) 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;
(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.7. Screening, recruiting, or determining eligibility (see section §46.116 (g) of the 2018 Common Rule at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116)

8. Posting of clinical trial consent form (see section §46.116 (h) of the 2018 Common Rule at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116)

9. Preemption (see section §46.116 (i) of the 2018 Common Rule at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116)

10.Emergency medical care (see section §46.116 (j) of the 2018 Common Rule at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116)

11. Consent for Children and Assent of Minors

    Parents or Guardians must consent for their children to participate in research in most cases. The IRB requires that the assent of a child subject is sought, if in its judgment the child is capable of making an informed decision about participating in the research. See RI-20-VIII. for definitions of child and minor in North Carolina.

12. Emancipated Minors

    In North Carolina, an emancipated minor may consent to medical or hospital care and/or treatment for themselves and for their children [CVHS RI-12]. The decree of emancipation must be provided to the investigator prior to consenting the emancipated minor as a subject in research except as described below. See RI-20-VIII for the definition of an emancipated minor.

13. Exceptions Involving Minors

    The General Statutes of the State [90-21.5] provide for a minor to legally consent to certain clinical services. For the proposed research, if the involvement of human subjects consists of the following interventions or interactions [CVHS RI-12], then minors may be considered adults for this purpose:

    a. A minor may consent for treatment of sexually transmitted disease or for alcohol or drug abuse.
    b. An unwed pregnant minor may consent to medical or surgical procedures relating to her pregnancy.

c. A minor mother may consent to the performance of medical or surgical care or services for her child.

G. Suspension or Termination of IRB-Approved Research
1. The IRB is authorized to suspend or terminate approved research:
a. That is not being conducted in accordance with the IRB's requirements; or
b. That has been associated with unexpected serious harm to subjects.
2. When suspension or termination action is taken, the IRB promptly reports its action to the investigator in writing including the reason(s) for the action.

H. Withdrawn Research
1. In the case a research application is submitted to the IRB for review and the investigator decides against conducting the study, he/she is required to inform the IRB.
a. If the study was never approved, the IRB will document its withdrawal.
b. If the study was approved, the IRB will document its closure.
2. It is the investigator's responsibility to inform all consented subjects of the study's closure.

VI. DOCUMENTATION

A. Documentation of Review
1. Board decisions are documented per federal regulations in the minutes and investigator correspondence:
a. Review procedure(s);
b. Informed Consent to include waiver status if applicable.

B. IRB Records
1. Investigator submitted documents, e.g. research applications, , progress reports, protocol amendments, and/or reports of unanticipated problems and/or adverse events as well as statements of significant new findings that are provided to subjects by investigators become permanent IRB records upon submission.
2. The IRB prepares and maintains documentation of its activities, to include:
a. Minutes of the IRB meetings in sufficient detail to show:
(i) Attendance to include which members, if any, were present via conference call and that the criteria for a member's participation in this manner have been satisfied;
(ii) Separate deliberations, actions, and votes for each protocol undergoing initial or continuing review by the convened IRB to include the basis for requiring changes in or disapproving the research; and a summary of the discussion of controversial issues and their resolution;
(iii) The vote on all IRB actions including the number of members voting for, against, abstaining and recusal, if applicable, ensuring maintenance of a quorum.
Examples of an acceptable format for documenting votes on actions taken by the IRB follow:
Total = 15; Vote: For-14, Opposed-0, and Abstained-1

Total = 14 (1 member rescued-provide name); Vote: For-12, Opposed-2.

c. IRB-investigator correspondence
d. Official documents of the IRB, e.g., FWA, IORG
e. IRB policy and procedures.

3. IRB records are retained for at least seven years electronically.
4. All records are accessible for inspection and copying by authorized representatives of HHS and FDA at reasonable times and in a reasonable manner.

C. Documentation of informed consent

1. Except as provided in paragraph (3) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the informed consent form
2. Except as provided in paragraph (3) of this section, the informed consent form may be either of the following:

(a.) A written informed consent form that meets the requirements of General Requirements for Informed Consent §46.116 (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116). The investigator shall give either the subject or the subject's legally authorized representative adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative.

(b.) A short form written informed consent form stating that the elements of informed consent required by §46.116 (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html#46.116) have been presented orally to the subject or the subject's legally authorized representative, and that the key information required by §46.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the subject's legally authorized representative, in addition to a copy of the short form.

3. An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

a. (i) That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential

harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;
(ii) That 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; or
(iii) If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

b. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

VII. INVESTIGATOR GUIDELINES

A. Research Application Components
   1. Full research protocol submitted utilizing the standard application form, which is available at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx ;
   2. Proposed informed consent document(s) or consent waivers request form, and if applicable foreign language consent and translation certificate and/or equivalent;
   3. Relevant funding information, if existent;
   4. Recruitment materials/advertisements intended to be seen or heard by potential subjects;
   5. Human subject protection education completion certificate/record;
   6. Evidence of current Health Insurance Portability and Accountability Act (HIPAA) compliance;
   7. Additional documents as indicated on the application as appropriate for the proposed research.

B. Investigator Responsibilities
   1. Complete human subject protection education and HIPPA education.
   2. For FDA-registered clinical trials, study sponsor training is required for investigator(s) and appropriate study personnel. Good Clinical Practice (GCP) training is desirable for clinical trial personnel.
   3. Assure the proposed informed consent form (ICF) conveys information in language understandable to the subject, does not contain any exculpatory language, and contains all the basic elements of informed consent and any additional elements (http://www.hhs.gov/ohrp/policy/consentckls.html) as appropriate. If waiver of informed consent or waiver of documentation of informed consent is desired, submit an Informed Consent Waivers Request. If the research involves children, submit a parent or guardian consent form and a child assent form if the child is capable of making an informed decision about participating in the research.
   4. Include the following human rights statement in the ICF: "The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If

you have any questions concerning your rights as a subject, email the IRB at irb@cvmc.us or telephone 828-326-3053. When subjects are being consented for registered clinical trials, also include the following statement: "A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

5. Submit your research application to the Administrator for Research and Evidence-Based Practice for review prior to submission to the IRB at research@cvmc.us.
6. Submit a complete signed research application to the IRB, following approval from the Administrator for Research and Evidence-Based Practice, via irb@cvmc.us
7. Only the IRB, using the guidance of federal regulations, can make a determination that proposed research is exempt from IRB review, NOT an investigator.
8. Attend convened meetings of the IRB if requested by the Chair to provide a study synopsis and answer questions.
9. Ensure each subject's understanding of the research and informed consent.
10. Provide subjects with a copy of the signed, dated and witnessed consent form; when appropriate, place a copy of the signed, dated and witnessed consent form in the subject's medical record; and keep the original signed, dated and witnessed consent form in your research records.
11. Submit progress reports as outlined by the IRB prior to expiration of your research study approval period. A standard form is provided at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx
12. Ensure records related to conduction of the research are retained for at least three (3) years following completion of the research.
13. Submit changes to the approved study protocol and/or INF to the IRB using the Study Amendment Form or provided at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx. Implement the changes only following written notification delineating subsequent IRB approval of the changes.
14. Report unanticipated problems and unanticipated adverse events if they occur during the course of the research to the IRB Chair by email or phone within 24 hours and in writing within 7 days. The report is to include a complete description of the problem or event, your assessment and basis for the assessment of whether the problem or event is study-related, and a statement addressing whether the research protocol or consent needs to be altered as a consequence of the problem or event. Refer to the Reporting of Unanticipated Adverse Events and Unanticipated Problems section of this policy [RI-20-V.E.] for determining what constitutes reportable unanticipated problems and unanticipated adverse events.
15. If for any reason the IRB suspends or terminates your approved research, you must abide by the IRB's decision and immediately cease research activity.
16. Should you decide against following through with research submitted to and/or approved by the IRB, you must inform the IRB of your intentions by submitting a Study Withdrawal Form available at https://www.catawbavalleyhealth.org/Medical-Center/Services/IRB-and-Human-Subjects-Research.aspx

VIII. DEFINITIONS

Adverse Event- any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, (e.g., 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.

Assent- a child's affirmative agreement to participate in research. Mere failure to object may not, absent affirmative agreement, be construed as assent.

Child- person who has 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.

Clinical Investigation- 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 FDA.

Emancipated Minor- a juvenile possessing a decree of emancipation, or a married juvenile has the same right to make contracts and conveyances, to sue and to be sued, and to transact business as if he/she were an adult according to Article 35 of Chapter 7B of the General Statutes of the State of North Carolina.

Guardian- an individual who is authorized under applicable State or local law to consent on behalf of a child to participate in research.

Family member- 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.

Human Device Exemption (HDE)- a premarket approval application submitted to and approved by the FDA for a human use device.

Human Subject-

a. a living individual about whom an investigator (whether professional or student) conducting research: (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [OHRP definition].
b. 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 participant or a patient. [FDA definition].

Human Use Devices (HUD)- medical devices intended to benefit patients in the treatment or
diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year.

Informed Consent- the voluntary choice of an individual to participate in research based on an accurate understanding of its purposes, procedures, risks, benefits, alternatives, and any other factors that may affect his/her decision to participate.

Interaction- communication or interpersonal contact between investigator and subject.

*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.

Investigator- 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.

Legally Authorized Representative- an individual, 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.

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

Minor or Unemancipated minor - any person under the age of 18 who has not been married or has not been emancipated [NC General Statutes – Chapter 90 Article 1A].

More Than Minimal Risk- the probability and magnitude of harm or discomfort anticipated in the proposed research <u>are</u> greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests.

Parent- a child's biological or adoptive parent.

Private information- information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public, e.g., a medical record. *Private information must be individually identifiable,* i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information, in order for obtaining the information to constitute research involving human subjects.

Protocol- detailed plan of the study.

*Research***-** systematic investigation designed to develop or contribute to generalizable knowledge.

Sponsor- a person who initiates a clinical investigation but who does not actually conduct the investigation.

Sponsor-Investigator- an individual who both initiates and actually conducts, alone or with others, a clinical investigation.

Test Article- 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 Public Health Service Act.

Unanticipated Problem involving risks to subjects or others- any incident, experience, or outcome that meets all of the following criteria: (1) unexpected, in terms of nature, severity, or frequency, given the research procedures that are described in the protocol-related documents (such as the IRB approved research protocol and informed consent document), and the characteristics of the subject population being studied; (2) related or possibly related to a subject's participation 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) related to the research than was previously known or recognized.

Vulnerable Populations- subjects likely to be vulnerable to coercion or undue influence, e.g., children, prisoners, pregnant women, mentally disabled persons, economically or educationally disadvantaged persons, incompetent adults (developmentally disabled, cognitively impaired elderly, unconscious or inebriated individuals).

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

IX. REFERENCES & RESOURCES

http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

http://www.hhs.gov/ohrp/policy/populations/index.html

http://www.hhs.gov/ohrp/policy/consentckls.html

http://www.hhs.gov/ohrp/policy/expedited98.html

http://www.hhs.gov/ohrp/policy/exprev.html

http://www.hhs.gov/ohrp/policy/continuingreview2010.pdf

https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/recent-final-medical-device-guidance-documents

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