LEGACY RESEARCH INSTITUTE

HUMAN SUBJECT RESEARCH PROGRAM

LEGACY IRB STANDARD OPERATING PROCEDURES

&

POLICIES

2026

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PART A: HUMAN RESEARCH PROTECTION PROGRAM (HRPP) AND INSTITUTIONAL REVIEW BOARD (IRB) STRUCTURE

1. **HRPP PURPOSE:** The Legacy Research Institute (LRI) Human Research Protection Program (HRPP) implements the Legacy Health human subject research protection program and required mechanisms to assure that studies involving the use of human subjects are in full compliance with the policies and regulations of Legacy Health, the Department of Health and Human Services (DHHS), the Federal Food and Drug Administration (FDA), the Office of Civil Rights (OCR), and Oregon State Law. Ensuring that protections for human subjects in research are implemented includes review of research according to legal, regulatory, ethical, bio-ethical, professional, and scientific standards, as well as Legacy Health policies and procedures. To assure those protections, research at Legacy which involves human subjects are without exception reviewed by the Legacy Institutional Review Boards (IRB) according to its human research protection program (HRPP) requirements. Review of human subject research includes full board review, expedited review, exemption determinations, determinations that proposed research is not human subject research, case studies, and quality improvement programs that are exempt from IRB review and oversight but that request or need a formal determination that the project is exempt from IRB oversight.
2. **HRPP ELEMENTS.** The key element of a HRPP program is a duly constituted and registered institutional Review Board (IRB). An IRB is responsible for the review and approval of all research involving human subjects that utilize Legacy Health (LH) facilities, sites, resources, or patients. The IRB is a federally mandated ethics and research review board charged with protecting the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable LH policies and federal and state regulations. The IRB is responsible for reviewing, approving, and monitoring all research projects involving human subjects.
3. **HRPP SCOPE.** Human research protection is a collaborative effort between all who develop, conduct, review, approve, and facilitate human research. It includes institutional leaders, the Institutional Review Board (IRB), Legacy Health researchers, key departments facilitating the conduct of research, LRI researchers, staff, and management. The HRPP aims to protect the rights and welfare of research participants by providing support, guidance, and education to facilitate research that is ethical, scientifically sound, and consistent with the mission of Legacy Health.
4. **PURPOSE OF THE IRB.** The purpose of the Legacy and LRI IRB's is to assure the conduct of all research activities and reviews of studies involving human volunteers and patients within Legacy Health are uniform, and in compliance with all applicable policies, regardless of funding source or relationship of the research investigator to the institution, to ensure protection of human subjects in biomedical and clinical research, to assure that studies involving the use of human subjects are in full compliance with the policies and regulations of Legacy Health, the Department of Health and Human Services (DHHS), the Federal Food and Drug Administration (FDA), and Oregon State Law, to assure that all research proposals which involve human subjects are without exception reviewed by the Legacy Institutional Review Board (IRB) unless review is ceded to another IRB per a cooperative agreement, and to establish the conditions under which protected health information ("PHI") may be used or disclosed by Legacy Health for research purposes.

5. **SCOPE OF LEGACY IRB OVERSIGHT.** Legacy IRB has review jurisdiction over all research conducted at Legacy departments and institutions, or uses Legacy patients as subjects, collects data and records from Legacy operations, obtains data about the subjects of the research through intervention or interaction with them, obtains identifiable private information about the subjects of the research, or conducts the informed consent of human subjects for the research. Legacy IRB may retain or exercise jurisdiction over all research even where it engages in cooperative agreements to waive, cede, or defer oversight to another or external IRB. LH includes Legacy Emanuel Medical Center, Randall Children's Hospital at Legacy Emanuel, Legacy Good Samaritan Medical Center, Legacy Mt. Hood Medical Center, Legacy Meridian Park Hospital, Legacy Salmon Creek Medical Center, Legacy Research Institute, Silverton, and all the Legacy clinics and partnerships.
6. **IRB RESOURCES.** LH may maintain multiple IRBs; there is one that meets at Legacy Good Samaritan, and one that meets at Legacy Emanuel. Good Sam and Emanuel IRBs are primarily tasked to review biomedical and hospital practice research. However, all IRBs can review research for any Legacy facility if membership of the IRB meets regulatory requirements for quorum and expertise.
7. **HUMAN SUBJECT IN RESEARCH ETHICS.** The origins of human subjects in research protection regulations are based on international standards such as the Nuremberg Code, the Geneva Convention and the Helsinki Accords. In the United States the regulatory framework was created with the drafting of the Belmont Report in 1978. Because of its involvement with the National Institute of Health, Good Samaritan established an IRB in 1981 while Emanuel established an IRB in the late 1980s due to its physician's use of products regulated by the Food and Drug Administration (FDA).
8. **FEDERAL WIDE ASSURANCE.** LH maintains Federal Wide Assurances with the Department of Health and Human Services' Office for Human Research Protection (OHRP). That assurance (FWA 00001280) commits LH to comply with applicable federal regulations governing the conduct of all research involving human subjects and is reiterated at Legacy in administrative policy LH100.18. Federal regulations include 45CFR46 (HHS) and 21CRF50 (FDA). OHRP provides oversight through the assurance process and education while FDA provides oversight through audit.
9. **IRB STRUCTURE.** Per the Common Rule and FDA requirements Legacy Health IRBs will operate via the HRPP program at Legacy Research Institute. The Legacy Health VP of Research will be the Institutional Official (IO) having oversight of LH IRBs.
10. **IRB MEMBERSHIP.** Per the Common Rule the membership of each IRB consists of at least five members, who are appointed by the IO. At a minimum, to assure diversity, the membership of the Board must include representatives from the following areas: 1.) scientific; 2.) non-scientific; and 3.) community. Board members are appointed as needed and serve at the discretion of the IO. Each IRB has a Chair and Vice-Chair who serve at the discretion of the IO. The members of the IRB must have expertise in the specific areas of review.
11. **IRB MEETINGS.** At LH there are two IRBs. Meetings of IRB are typically held once per month or more as needed. Meetings may be cancelled or rescheduled contingent on workload and scheduling needs. The IRB Administrator or Chair may call an additional meeting if indicated. A majority plus one of the IRB constitutes a quorum, which includes at least one member whose primary concerns are in nonscientific areas.

12. **DECISIONS AND DETERMINATIONS OF THE IRB.** Decisions by the IRB are by majority vote of members. A member at the meeting having a significant conflict of interest (e.g., as principal investigator, co-investigator, or study staff) may not vote on that matter. A member with a conflict of interest may be in attendance to answer questions related to the study.
13. **REQUIRED REGULATORY FINDINGS OF THE IRB.** The IRB is tasked to make certain regulatory findings for research under FDA jurisdiction (drugs, devices, and biologics), OHRP jurisdiction (federally funded), for certain vulnerable populations (prisoners, minors, pregnant women/fetuses). Regulatory determinations will be documented by methods that adequately preserve and document the required regulatory findings.
14. **ACTIONS OF THE IRB ON PROPOSED RESEARCH.** The IRB reviews research proposals submitted to it and shall periodically conduct ongoing or continuing review of approved research projects. Consideration will be given during the approval process by the IRB to determine the review frequency for the study.
15. **EXEMPT FROM REVIEW.** The Common Rule identifies six categories of research that may be eligible for exemption from IRB review. The LH IRBs apply these six exemption categories only to protocols determined to be no more than minimal risk. If an investigator believes his or her research falls into one of these exemption categories, he or she must still submit a protocol to an IRB. Only an IRB can determine whether the research is exempt from review. The IRB has the right not to exempt a protocol and to require full review by the convened IRB or expedited review by an IRB member, particularly if the research involves a sensitive population or sensitive topic.
16. **EXPEDITED REVIEW.** The Chairs or Vice-Chairs and other designated reviewers may review and approve minor amendments or studies that involve no more than minimal risk to the subject as specified in the Common Rule. If they are unable to approve those studies or amendments, they must instead be referred to the full IRB for consideration. Continuing reviews of projects are conducted by full Board meetings unless they involve minimal risk or have not yet enrolled any subjects and then may receive expedited review. The IO, Chairs or Vice-Chairs may delegate these reviews to any other member of the IRB that they deem qualified.
17. **ADMINISTRATIVE AMENDMENTS.** IRB administrative personnel (Research Regulatory Specialist, IRB Coordinator) designated as expedited reviewers, may approve any administrative amendments, i.e., those amendments that do not directly affect patient risk or are minor changes to the research.
18. **PARTICIPATION OF NON-MEMBERS.** Persons who are not members of the Board may attend the meetings with the consent of the Regulator Specialist with notice to the Chair. If non-members are actively involved in a protocol being discussed, they must excuse themselves from the meeting prior to voting. The IRB may invite individuals with competence in special areas to assist in the review of complex issues that are beyond the expertise of the IRB. These individuals may not vote as part of the IRB. The presence of the PI or study staff at the IRB meeting is not mandatory but is encouraged in order to provide the PI the opportunity to answer questions. The PI is asked to leave the room during the deliberation and voting.
19. **FUNCTIONS OF THE IRB.** The IRB is tasked with ensuring the rights and safety of the research subject. Research projects should be reviewed in a manner so as to provide for the protection of the subject against undue or unnecessary invasion of privacy, disregard for

human dignity, and physical, psychological or social harm. Decisions to approve research proposals is based on weighing the risks to the subject and comparing them to the potential benefits to the subject plus the potential benefits to generalizable knowledge. Once the IRB has determined that such risks and benefits are relatively equal, then they must ensure that subjects are presented with appropriate information during a consent process that will allow them to make an informed decision concerning participation.

20. **RESPONSIBILITIES OF THE CHAIR.** Each IRB Chair, and when appropriate the Vice-Chair, are responsible, when requested, for the following:

    - Conducting the IRB meeting in a fair and unbiased manner
    - Review investigational treatment requests in emergency situations
    - Considering expedited initial review of minimal risk studies
    - Expedited review of protocol modifications that do not increase the risk to the subject
    - Determine exemption status for activities submitted for review
    - Review on-site new/unexpected serious adverse events
    - Provide liaison/communication to the PIs as needed
    - Provide liaison/communication to LH medical staff committees/individuals as needed
    - Consult with the IO and/or the IRB Administrator on whether to immediately suspend studies due to unexpected serious hazards to research subjects, with notice and full review by the full IRB as soon as possible
    - Consult with the IO and/or the IRB Administrator on whether to immediately suspend studies due to investigator non-compliance and/or protocol violations that are serious in nature and/or represent a pattern of misconduct, with notice and full review by the full IRB as soon as possible
    - Consult with the IO and/or the IRB Administrator on whether to cede jurisdiction to another IRB per request for single IRB oversight or central IRB oversight.

21. **REVIEW PROCESS.** A primary and secondary reviewer system is utilized for the review of proposals, meaning that two members of the committee will summarize the proposed research for the IRB. However, all members will receive all items relevant for review, except where there is an exceptionally large investigator brochure (IB) that cannot practicably be sent to all members; in that instance, only the primary and/or the scientific reviewer will receive the IB for review and summary provided by the primary and secondary reviewers. (All members will be notified that the primary or scientific reviewer received the IB and will review and summarize as needed.) Where there are a large number of advertisements or subject materials for review, a third reviewer may be added whose primary responsibility is to review those items and summarize them for the committee. All reviewers may receive submitted documents for review, which should include the following for ensuring adequate review:

    - IRB Questionnaire/Application form
    - Written Protocol
    - Consent forms
    - Assent forms
    - Other consent documents
    - Advertisements and subject materials
    - FDA correspondence regarding drugs, devices, etc. CV of the principal investigator,

- CITI training documentation for PI. CITI training for other study staff may be requested, which the PI must attest has been completed.

22. **RETENTION OF IRB RECORDS.** All IRB records will be retained for at least 3 years. Records relating to research that is conducted shall be retained for at least 3 years after completion or closure of the research. The IRB maintains both paper and electronic documentation of IRB activities, including the following:

    - Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.
    - Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.
    - Records of continuing review activities.
    - Copies of all correspondence between the IRB and the investigators.
    - A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.
    - Written procedures for the IRB as required by regulatory provisions.
    - Statements of significant new findings provided to subjects as required by regulatory provisions. The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

23. **COMMUNICATION WITH PRINCIPAL INVESTIGATORS AND SPONSORS.** The IRB office may communicate decisions of the IRB in any manner best calculated to apprise the PI of the IRB actions on pending research. The means to communicate and document the information given to the PI or study staff may be via email, phone, letter, or a “Board Action” form. Communications to the PI are crafted by the Legacy senior regulatory analyst with input as needed from the IRB Chair or another member. The communication should provide the detailed circumstances of approval, disapproval or tabling of the proposal. Such communication is sent to the PI and/or the relevant study coordinator. Communication to sponsors is appropriate and such communication is not prohibited, though the IRB does not typically communicate directly with sponsors unless the investigator is unable to provide information requested by the IRB.
24. **IRB COMMUNICATION TO LEGACY ADMINISTRATION.** The IRB packets for board review, IRB training, minutes and agenda are distributed to the IO and other interested stakeholders as directed by the IO. The information is sent via email prior to a scheduled IRB meeting and will contain both new and older research review documentation. The IO may

request additional information and has full access to IRB documentation held electronically and in paper form.

25. **IRB COMMUNICATION OF EXPEDITED REVIEW ACTIVITIES.** The IRB will be kept informed of expedited approval and exemption determinations as well as deferral arrangements with external or central IRBs, as well as emergency use via a section of the IRB agenda entitled “Information”. Such “Information” will be distributed to the IRB in a timely manner in the IRB review packets and will contain paperwork that describes items that did not reach full board review. Any member of the IRB can request more details about such items and can initiate discussion as to whether such items should be reviewed by the full board, even in those circumstances where the item has already been approved via expedited review.

LEGACY RESEARCH INSITITUTE – POLICIES AND PROCEDURES 2026

DOMAIN 000: DEFINTIONS

001: DEFINITIONS:

"Allegation of Noncompliance": An unproven assertion of "Noncompliance".

"Children": 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.

"Clinical Investigation": Research as defined by FDA".

"Clinical Trial as Defined by 45 CFR §46": 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.

"Committee Review": Processes that require a convened IRB.

"Compassionate Use": The use of an unapproved device on an individual who has a life-threatening or serious disease or condition and no generally acceptable alternative treatment for the condition exists.

"Conflicting Interest": An IRB member or consultant has a conflicting interest if any of the following are true for the member/consultant or an individual in the member's "Immediate Family":

- Involvement in the design, conduct, or reporting of the research,
- Equity interest "Related to the Research", exclusive of interests through mutual funds,
- Compensation "Related to the Research" in the preceding 12 months,
- Proprietary interest "Related to the Research", including copyrights, or patents, trademarks,
- Any other reason for which the IRB member believes that he or she cannot be objective.

"Continuing Noncompliance": A pattern of "Noncompliance" that is likely to continue without intervention or failure to work with the IRB to resolve "Noncompliance".

"Designated Reviewer": An "experienced IRB member" designated by the LRI IO to conduct "expedited, administrative or exempt.

"Emergency Use": The use of an unapproved drug, biologic, or device on an individual in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

"End Approval Date": The last date that a study is IRB approved and the last date that a study can be conducted without undergoing continuing review.

"Engaged in research": Legacy is engaged in research when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

"Experienced IRB Member": An IRB member who has gained over a period of time sufficient knowledge and skill in conducting IRB reviews and to serve as "Designated Reviewer".

"Expiration Date": The day after the "End Approval Date".

"Fetus": The product of conception from implantation until delivery.

"Guardian": An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

"Human Subject (FDA)": An individual who is or becomes a participant in "Research as defined by FDA", either as a recipient of the test article or as a control, or an individual on whose specimen an investigational device is used.

"Human Subject (OHRP)": A living individual about whom an investigator conducting research obtains

(1) data through "Intervention" or "Interaction" with the individual, or

(2) information that is both "Identifiable Information" and "Private Information".

Or

Obtains information or biospecimens through "Intervention" or "Interaction" with the individual, and uses, studies, or analyzes the information or biospecimens; or

Obtains, uses, studies, analyzes, or generates "Identifiable Private Information" or "Identifiable Biospecimens".

"Identifiable Private Information": "Private Information" for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

"Identifiable Biospecimen": A biospecimen for which the identity of the "Human Subject as Defined by HHS" is or may readily be ascertained by the investigator or associated with the biospecimen.

“Immediate Family”: Spouse and dependent children.

“Impartial Witness”: A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the entire consent process and reads the consent document and any other written information supplied to the subject as part of the consent process.

“Institutional Review Board (IRB)”: A board charged with protecting the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable Legacy policies as well as state and federal regulations.

“Interaction”: Communication or interpersonal contact between investigator and subject

“Intervention”: Physical procedures by which information or biospecimens are gathered and manipulations of the subject or the subject’s environment that are performed for research purposes.

“Investigator” means an individual who conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Sub-investigator" includes any other individual member of that team. 21 CFR 312.3

- A “Qualified PI” is someone who has the training and qualifications to conduct the study.
- A “PI” is the person fully responsible for the proper conduct of the study.
- A “Co-PI” is a co-investigator of the PI who also takes full responsibility for the conduct of the study.
- A “Sub-PI” is a person who is part of the study staff and works for the PI.
- Co-PI’s should be avoided if possible and one PI with Sub-PI’s are preferred to ensure that one investigator takes full responsibility for the study. However, with an adequate rationale, the IRB may approve multiple PI’s if all are willing to be responsible for the conduct of the study.

“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 by 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.

“Non-significant Risk Device”: An investigational device that is not a Significant Risk Device.

"Noncompliance": Failure to follow the regulations or the requirements or determinations of the IRB.

"Prisoner" minimal risk: 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.

"Prisoner": Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

"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 that has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public.

"Protected Health Information": Any information that 1) is received by a health care provider, health plan, or clearinghouse, 2) is transmitted electronically or maintained in any other form or medium (including oral), 3) relates to the provision of or payment for health care for a patient or to the past, present or future physical or mental health condition of a patient, and 4) is individually identifiable.

"Qualified Study Staff" are study team members that have the required training to participate in the conduct of the study i.e., CITI or equivalent.

"Reliance Agreement": Documentation describing the reliance of an institution on an IRB for the oversight of research and the responsibilities that each entity will undertake to ensure compliance with regulatory requirements, which can be embodied in a written agreement between the institution, an institution-wide policy directive, or a research protocol.

"Research per FDA": Any experiment that involves a test article and one or more Human Subjects as defined by the FDA, and that must meet the requirements for prior submission to the Food and Drug Administration

"Research": A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

"Serious Noncompliance": Noncompliance that adversely affects the rights and welfare of subjects.

"Significant Risk Device": An investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

"Single Patient Expanded Access": Treatment with an investigational drug under an IND where the FDA granted an IND.

"Study Staff" are all personnel working for the PI that are involved in regulatory aspects of the study, involved in the consent process with subjects, recording study data, involved in the submission of adverse event reports, or other processes specific to the research. Medical staff that are not involved in study related processes but instead are providing standard clinical services do not have to be considered study staff. However, if there is any doubt about whether medical staff should be considered study staff, the PI should ensure that staff are trained in human subject research protection i.e., CITI or equivalent.

"Suspension of IRB Approval": Temporary or permanent withdrawal of IRB approval for some or all research procedures short of termination of IRB Approval.

"Termination of IRB Approval": Withdrawal of IRB approval for all research procedures such that the study is permanently closed.

"Test article": 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 FDA.

"Unanticipated Problems Involving Risks to Subjects or Others": Information that:

- Is unexpected (inconsistent with information previously reviewed by the IRB); and
- Indicates that subjects or others are at increased risk of harm because of the research study.

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

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DOMAIN 1: QUALIFIED PRINCIPAL INVESTIGATOR

101. Principal Investigator Qualifications and Expertise
102. PI and Study Staff Training and Qualifications
103. Change in PI
104. Submissions by the PI
105. PI and Study Staff Disclosures of Conflicts of Interest

101: PRINCIPAL INVESTIGATOR (PI) QUALIFICATIONS AND EXPERTISE

The PI for the proposed study must be qualified to conduct the study. The approved PI is responsible for all aspects of the conduct of the research.

The PI must submit a current CV as proof of qualification and expertise for the conduct of the research. There should be one named PI for the research; Co-PIs are equally responsible for the conduct of the research and must submit separate applications if the intent is to have Co-PIs in the research.

a. The PI must provide information to the IRB such that the IRB is able to ascertain the acceptability of proposed research in terms of standards or professional conduct and practice. 21 CFR 56.107(a) and 45 CFR 46.107(a).

   The PI must provide information, when requested, regarding any history of the PI in being audited by the FDA, suspensions, or other issues related to research non-compliance, and any corrective actions taken as a result of such audits, etc.
b. The PI must have permission for the conduct of the research from the appropriate Legacy Health manager of the department in which the research will be take place.

c. Non-Legacy researchers must have Legacy management authorization to conduct the research at a Legacy site using Legacy patients either via a Legacy manager, co-investigator, or sub-investigator. Non-Legacy researchers must also provide assurance that a Legacy staff physician will provide medical responsibility for study subjects and will provide assurance from that Legacy physician that they assume medical responsibility for the subjects, if applicable:

102: PI AND STUDY STAFF TRAINING AND QUALIFICATIONS

a. The PI should have available an adequate number of qualified staff and adequate facilities for the duration of the trial to conduct the trial properly and safely. GCP 4.2.3.

b. LH requires that all PIs complete an educational tract (CITI) every three years that is focused on protecting the rights and safety of the research subject.

c. The Collaborative Institutional Training Initiative (CITI) from the University of Miami provides a research ethics education that is necessary to conduct clinical trials and to communicate effectively with the Legacy IRB. The training is tailored to the individual's role in the research study. Investigators may substitute similar educational tracts that are

offered by the NIH, FDA, or any other clinical trial sponsor or agency. Any individual who works with human research subjects may take the CITI training, but it is the responsibility of the PI to ensure that all such personnel are familiar with the material offered and maintain a record of their certification.

d. The PI must designate all research staff on the IRB application, including co-investigators, collaborators, and study coordinators, and ensure that they have received training in human subject research protection.

e. In all studies for which the PI is not licensed, credentialed, and privileged at LH to perform all proposed interventions, the PI must designate a co-investigator with expertise in the relevant medical specialty. In addition, if the PI cannot respond to emergencies experienced by participants, an appropriate clinician must be designated as the responsible clinician for the study and will be responsible for all participant safety issues, including checking all laboratory/study testing in the research; following all laboratory/study results and communicating all moderate or severe results to the study participant, the study participant's primary care and specialty physicians; and assuring the accurate recording of all relevant laboratory/studies in the participant's electronic medical record.

f. Investigators and clinicians must maintain appropriate professional credentials and licensing privileges. The IRB may request additional information from investigators, study staff, and participating physicians, such as curricula vitae, to ensure the qualifications of the research team are appropriate for the proposed study.

103: CHANGE IN PI

a. If a PI is leaving an approved research study, either permanently or temporarily, e.g., on sabbatical, prior to the current PI's departure, for illness or other reasons, the PI must submit a modification of the research and request for a new PI to oversee the study.

b. The PI should submit information that clearly indicates who is assuming responsibility for the research in the PI's absence, with information from the new or temporary PI specifically attesting that they are assuming all responsibility for the conduct of the research.

c. No study may be conducted without an approved PI; all research must be voluntarily suspended during the approved PI's absence.

d. If the PI fails to provide for a change in PI during an absence or fails to suspend the research voluntarily during the PI's absence, the IRB may find grounds for non-compliance or serious non-compliance and administratively close the study.

e. The PI must personally conduct or supervise the research, and the conduct of the research as a whole cannot be delegated to study staff.

104: SUBMISSIONS BY THE PI

a. For review of a proposed study, the PI must submit the following information:

- Submission of the appropriate Legacy Research Institute (LRI) Application form
- Submission of a written protocol
- Submission of a consent/assent form (or a request for a waiver of consent or waiver of a consent form)
- PI CV – updated and current
- Documentation of CITI or equivalent training in human subject research protection
- Research "subject materials" to be used in the research, such as advertisements, recruitment materials, etc.
- PI office and contact information
- Study Sites
- Study services or procedures to be conducted (acceptable to describe in protocol or consent form)
- PI's role and professional capacity at Legacy Health
- Documentation or attestation that a Legacy Manager has granted permission to conduct the proposed study in the department where the research will be conducted
- Detailed information regarding study staff and confirm their human subject research training
- Conflict of Interest Disclosure information
- Sponsor Information

b. All PIs must attest and agree to the following for IRB approval of the proposed research:

- Obtain approval before conducting research and stop research if approval is suspended or lapses. Submit each research project for initial and continuing review and approval. Do not conduct research until the PI has received approval from the IRB office.
- Complete all educational requirements for conducting research, assure that all research staff under PI supervision have completed the same or similar requirements, and monitor all aspects of the approved study.
- Assure compliance with the approved protocol and all federal, state, and institutional regulations.
- For human research, ensure approved informed consent procedures are followed, obtaining all required signatures and giving a copy of the signed consent form to each participant.
- Protect all LH sensitive data, particularly data identifiable for any private individual. Assure paper and electronic LH sensitive data are only accessible to authorized individuals and storage and security are maintained as approved by the IRB.
- Report as required to the IRB any deviations, adverse events, unanticipated outcomes, and subject complaints.

c. Additional attestations by the PI may be required by Legacy IRB and may be added to relevant application forms at any time.

105: PI AND STUDY STAFF DISCLOSURES OF CONFLICTS OF INTERESTS

a. PI's and study staff Legacy must report any significant financial conflict of interest (COI). A COI may include a monetary value not limited to salary or other payments for services (e.g. consulting fees or honoraria), equity interests (e.g. stocks options or other ownership interests) and intellectual property rights that exceed $5,000 per annum if salary, fees or other continuing payments represent more than a 5 % ownership for any one enterprise.

b. PI's at Legacy will also report any financial benefits made available in connection with the conduct of a study that are in addition to the ordinary compensation for services, beyond customary and reasonable fees, including incentive pay, rewards for early recruitment, or bonuses for reaching enrollment goals.

c. Where the PI or study staff indicate a COI, the Legacy IRB is tasked with determining what action should be taken to manage that conflict. These actions may include but are not limited to:

- public disclosure of the conflict through inclusion in the consent form
- monitoring of the research project by independent reviewers
- modification of the research plan
- disqualification of the investigator from participating in all or a portion of any sponsored research including recruiting subjects and analysis of data
- divestiture of an investigator of any financial interest in any research sponsor

d. PI and study staff whose research is funded by the Public Health Service (NIH, AHRQ, CDC, FDA and others) are required to make yearly disclosures and to have undergone COI training through the CITI program.

DOMAIN 2: SUBJECTS OF THE RESEARCH

201. INCLUSION AND EXCLUSION OF SUBJECTS

a. The research protocol and/or application form must include inclusion and exclusion criteria that clearly indicate the intended age, sex, or gender identity of the subjects of the research. It must also include the duration of the research for subjects, the number of subjects intended to be enrolled in the research at Legacy and at national or international sites, and the total enrollment for the study.

b. The selection of subjects should be fair. In determining whether the targeted population for the study is equitable, the IRB will consider the purposes of the research and the setting in which the research will be conducted and will be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

c. The PI must advise the IRB of the planned enrollment of subjects, including their age, gender or gender identity, vulnerability and planned number to be enrolled at the site(s) where the research will be conducted. The PI must provide adequate information regarding the PI's planned enrollment of subjects by submitting the following (non-exhaustive) characteristics of the population under study:

- Adults
- Minors
- Females
- Males
- All Genders (including LBGTQ+)
- Other gender identities
- Age range
- Minor age range

- Mature Minors' age range
- Fetuses
- Pregnant women
- Prisoners
- Wards of the State
- Cognitively Impaired
- Unconscious
- Adult Subjects with Legally Authorized Representative (LAR)
- Poor/Uninsured/underinsured
- Non-English speakers
- Non-Readers
- Employees of Legacy
- Institutionalized
- Stigmatized or marginalized
- Sensitive or legal risks (sex abuse, drug users)
- Secondary Subjects
- Minorities or marginalized populations
- LBGTQ+
- Principal Investigator
- Study Staff

d. The inclusion/exclusion of subjects must be consistent among the application and protocol and any other study documents for approval to be granted. The written protocol is the controlling document for describing the inclusion/exclusion of subjects.

e. Adult subjects that cannot consent for themselves but intended to be enrolled will be considered vulnerable subjects, and the protocol must describe the rationale and circumstances for their inclusion into the research via a legally authorized representative (LAR). The rationale for enrolling subjects via a LAR must be consistent with Oregon law and must be ethically justified by the research. The IRB may exclude the use of LARs if it finds that their use is not ethically justified.

f. The PI must provide information about whether any subjects to be enrolled will be from vulnerable groups and must be prepared to give a justification or rationale for their enrollment. For example, if the research seeks to enroll pregnant women and their fetuses, prisoners, or minors, but there is no obvious reason why they should be enrolled, the protocol should detail a rationale for their inclusion. Mere convenience or reaching enrollment goals is normally not a sound reason for including vulnerable populations in research. However, where the research is minimal risk, merely collecting data on standard care practices and enrollment of vulnerable populations may be appropriate.

g. Exclusion of any adult subjects into the research must be described in the research proposal and a rationale for the exclusion provided. Examples of excluded groups might include minority groups, non-English speakers, transgender, etc.

202. VULNERABLE POPULATIONS: General

a. Enrollment of some populations requires special findings or determinations by the IRB. Certain groups of participants are considered to be particularly vulnerable to coercion or undue influence in a research setting. These groups, as outlined in the Common Rule, are children, wards of the state, prisoners, pregnant women and their fetuses, persons who are mentally disabled or otherwise cognitively impaired, and economically or educationally disadvantaged persons.

b. Vulnerable populations who must be protected from coercion may include patients facing life threatening diseases or who are recruited for research studies in emergency situations. The FDA regulations (21CFR 50.24) allow for research studies involving participants in emergency settings who are unconscious or otherwise incapable or providing informed consent.

c. In reviewing research studies involving all categories of vulnerable participants, the IRB must determine that their use is adequately justified and that additional safeguards are implemented to minimize risks unique to each group. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, the IRB shall ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects.

d. Vulnerable populations by regulation are: children, prisoners, pregnant women and their fetuses, mentally disabled persons, or economically or educationally disadvantaged persons, or any group that are likely to be vulnerable to coercion. Required findings and determinations for some vulnerable populations are set out in additional regulations:

- Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research, 45 CFR 46.202(c), (d), (f) Definitions. (c) Fetus means the product of conception from implantation until delivery; (d) Neonate means a newborn; (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.

- Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects, 45 CFR 46.303 (c) Definitions. 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 that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

- Subpart D - Additional Protections for Children Involved as Subjects in Research, 45 CFR 46.402(a) Definitions. 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.

203. VULNERABLE POPULATION: Children

a. Definitions for Research Involving Children

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

- Children – Under Oregon state law, children are persons who are less than 18 years of age.

- Emancipated Minor – A legal status conferred upon persons who have not yet attained the age of legal competency as defined by Oregon state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self –support, marriage or procreation. Those who have had the disabilities of minority removed for limited or general purposes by the State of Oregon.

- Guardian – An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

- Permission – The agreement of parent(s) or guardian to the participation of their child or ward in research.

- Parent - a child's biological or adoptive parent.

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

b. Risk Determinations for Children are required.

IRB must determine whether the research can be approved under one of the following categories:

- Category 404 – No greater than minimal risk. Permission from one parent may be sufficient.
- Category 405 – Greater than minimal risk with the prospect of direct benefit to the child participating. The IRB may find that the permission of one parent is sufficient.
- Category 406 – Minor increase over minimal risk with no prospect of direct benefit to the child participating. Permission of both parents is required unless one parent has legal custody or one parent is deceased, unknown, incompetent, or reasonably unavailable.

c. **Assent and Parental Permission Requirements:** When research involves children, investigators must submit a child assent form and parental permission form in addition to the materials listed in the policy on initial review.

   The IRB shall review the parental permission documents and the plan provided by the investigator to ensure that these documents are signed by the parents or the legally appointed guardian of children under age 18. Parental permission documents should comply with the informed consent policy. The IRB must determine for each protocol whether the permission of both parents is necessary and the conditions under which one parent may be considered "not reasonably available."

   - **Minor's assent:** The IRB must determine for each protocol – depending on such factors as the nature of the research and the age, status, and condition of the proposed participants – whether all or some of the children are capable of assenting to participation, considering the ages, maturity, and psychological state of the children involved. In general, verbal assent should be obtained from children under the age of 7 whenever possible, and assent documents should be signed by participants 7 through 17 years of age, provided the child is mature enough to understand the planned intervention.

   - **Parent's permission:** The IRB shall determine that adequate provisions have been made for soliciting the assent of children and the permission of their parents or guardians. The IRB shall determine that if assent is sought, the information/explanation of the proposed research procedures be in a language that is appropriate to the child's age, experience, maturity, and condition.

   - **Minor's dissent/veto:** Generally, the child's dissent or veto of participation is sufficient to make the child ineligible for inclusion in the study. However, the parent or guardian, with IRB and physician approval, may override the veto if the intervention will benefit the child.

d. **Alteration or waiver of parental permission/assent:** The IRB may approve a consent procedure that does not include, or which alters, some or all the elements of informed consent, or waive the requirements to obtain informed consent provided that the IRB finds and documents that:

   - The research involves no more than minimal risk to the participants
   - The waiver or alteration will not adversely affect the rights and welfare of the participants
   - The research could not practicably be carried out without the waiver or alteration
   - Whenever appropriate, the participants will be provided with additional pertinent information after participation
   - The research is not subject to FDA regulation.

e. **Direct benefit to minor:** When the research offers the child the possibility of a direct benefit that is important to the child's health or well-being and is available only in the

context of the research, the IRB may determine that the child's assent is unnecessary. Assent may also be considered unnecessary if the capability of some or all of the children is so limited that they cannot reasonably be consulted. The IRB shall consider and document if additional measures are required when permission or assent is waived.

f. **Minors becoming Adults:** Minor participants should be re-approached after they attain their majority to confirm that they are still willing to participate in the research study, as demonstrated by the signing of an adult consent form.

g. **Wards of State:** Children who are wards of the State or any other agency, institution, or entity can be included in approved research only if it is either related to their status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

- The IRB shall require an advocate to be appointed for each child who is a ward.
- The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
- An individual may serve as an advocate for more than one child.
- The advocate must be an individual who has the background and experience to act in the best interest of the child and agrees to act in that interest for the duration of the child's participation in the research.
- The advocate must not be associated in any way (except as an advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

h. **Special Circumstances:** For some research activities, the IRB may require that an IRB member, research intermediary, or an advocate for the child be present during the assent and permission procedures to verify the child's understanding and to support the child's preferences. The IRB may also require that the parent(s) or a close family member be present during the research, especially if the child will be exposed to significant discomfort or inconvenience, or if the child will be required to spend time in an unfamiliar place.

i. **Wavier of Consent:** The IRB may waive or alter the consent process if it finds that the research is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the children who are subjects, and that the investigator provides appropriate alternate mechanism for protecting children who are subjects.

j.

204. VULNERABLE POPULATION: Pregnant Women/Fetuses

a. Subpart B of the Common Rule provides additional protections for research involving pregnant women and their fetuses. If the research will include pregnant women, IRB needs to determine whether all the conditions of subpart B have been met. Determine if the research provides for:

- A prospect of direct benefit to the pregnant woman.
- A prospect of a direct benefit both to the pregnant woman and the fetus.
- There is no prospect of benefit for the woman or the fetus when the 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.
- Whether consent is obtained in accordance with the informed consent provisions according to regulations.
- If the research suggests a direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accordance with regulations.
- For children who are pregnant, assent and permission are obtained according to state regulations for emancipation.

b. Minimal Risk to Fetus. Pregnant women should not normally be excluded from research if the risk to the fetus is minimal. If pregnant women are included in a research protocol, the informed consent must address the possible impact of the research on the fetus.

c. Pregnant Women Research. Researchers who conduct studies targeting conditions specific to pregnant women must obtain informed consent from both the pregnant woman and the father of the fetus; however, consent of the father is not necessary if:

- The purpose of the study is to meet the health needs of the mother.
- The identity or whereabouts of the father cannot be reasonably ascertained.
- The father is not reasonably available.
- The pregnancy is the result of rape.

d. Research involving the placenta, the dead fetus, or fetal material after delivery. When information associated with these materials is recorded for research purposes in a manner that living individuals, including the mother, can be identified, directly or through identifiers linked to those individuals, those individuals are research participants, and all human research protection relevant policies and policies apply.

205. VULNERABLE POPULATION: Prisoners

a. Definitions for Research Involving Prisoners:

- **Prisoner:** Prisoner means any individual involuntarily confined or detained in a penal institution, including individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. A "prisoner" is someone an adult or a minor, but minors are typically held in "detention" or may be held under a civil commitment type hold via juvenile court jurisdiction. A minor prisoner may or may not be a ward of the court, but the circumstances may require that the regulations governing research on wards also may need to be reviewed and considered by the IRB.

- **Minimal Risk:** Minimal risk for a prisoner means the probability and magnitude of physical or psychological harm that is normally encountered in their daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

b. General requirements:

- Research involving prisoners does not qualify for exemptions from IRB review.
- Approval of research involving prisoners must meet the requirements of Subpart C of the Common Rule and Oregon law.
- Specific regulatory findings are required for the inclusion of prisoners in research.
- When reviewing research involving prisoners, the IRB reviewing the protocol must include, as a member of the IRB, either temporarily or permanently, a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity.
- A PI may not enroll a prisoner in an ongoing IRB-approved study without the approval of the IRB. If a participant becomes a prisoner during a research study, the IRB must be notified.

c. Permissible Categories of Research with Prisoners:

- A study of the possible causes, effects, and processes of incarceration, and criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants.
- A study of prisons as institutional structures or of prisoners as incarcerated persons provided that the study presents no more than minimal risk and no more than inconvenience to the participants.
- Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis, which is much more prevalent in prisons than elsewhere, and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults).
- Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant.
- Epidemiologic studies whose sole purposes are either (i) to describe the prevalence or incidence of a disease by identifying all cases or (ii) to study potential risk factor associations for a disease.

206. OTHER VULNERABLE POPULATIONS:

Other subjects or subject populations not described in the regulations may nevertheless be vulnerable in the context of the proposed research. The Board may/should make findings of vulnerability where appropriate and may require the PI to provide additional protections or safeguards based on those findings before the research can be approved.

a. **Cognitively Impaired:** Research involving participants with diminished decision-making capacity will not be considered for exemption or expedition and must be reviewed by the full board.

- Research involving subjects with diminished decision-making capacity must specifically address how an individual's capacity to give informed consent will be determined. Examples of diminished decision-making capacity include: diagnosed mental retardation, some forms of mental illness, dementia, and coma, whether temporary, progressive or permanent.
- If an individual alternates between periods of mental competence and incompetence, the PI should obtain consent from the individual as provided and ask permission from the individual to obtain consent from a relative or other person who could otherwise grant legal consent for treatment in the event that the individual becomes incapable of continuing to make informed consent decisions in the future.
- If an individual asks to withdraw from a research study at any time, their participation in the research study must terminate, even if the investigator does not believe the individual to be competent to make informed decisions and even if a second opinion or third-party consent has been obtained.

b. **Economically or Educationally Disadvantaged:** For research involving economically disadvantaged participants, special care must be taken to ensure that any financial incentives offered do not represent the sole grounds for the individual's participation in the research protocol.

c. **Employees and Students as Participants:** In many research studies, employees or students are recruited as participants. PIs should be aware of possible coercion when using employees or students in their research. For example, if employees or students believe their participation (or lack of participation) will be made known to someone who holds power over his or her employment or academic status, the employee or student may perceive coercion. How the PI plans to handle potential problems of coercion and undue influence must be addressed when the study is submitted to the IRB. Usually, placing language into the consent form that informs employees or students that refusal to participate in the research will not impact their employment, etc., will be sufficient. Consider adding the following language to the consent form:

For Students: *"You may choose not to participate or to stop your participation in this research at any time. This will not affect your internship, class standing, or grades at Legacy or any Legacy department, and there will be no penalty or loss of benefits by your refusal to participate or a decision to stop participation in the research at any time."*

For Employees: *"Your participation in this research is in no way a part of your employment duties at Legacy, and your refusal to participate will not in any way affect your employment with Legacy or any Legacy department, and there will be no penalty or loss of benefits by your refusal to participate or a decision to stop participation in the research at any time."*

d. **Exceptions from Consent in Emergency Research:** Under 21 CFR 50.24, the FDA allows research without prospective consent under carefully controlled circumstances: unique emergency medical situations in which patients or family members cannot give informed consent before treatment and the need to allow emergency care to advance through research.

   According to FDA regulations, to qualify for an exception from informed consent:

   - The research study must involve participants suffering from a life-threatening disease process or injury for which the current standard of care is associated with a very high failure or mortality rate.
   - In addition, there must be reasonable evidence that the research has the potential to provide real and direct benefit to the patient.
   - Furthermore, studies must be held to the highest ethical standards. These clinical trials undergo multiple independent rigorous reviews to ensure that they meet these standards.
   - Before any patients are enrolled, communities are consulted about participation and made aware that informed consent will not be obtained for most study participants, as required by law.
   - Surviving patients and/or their authorized representatives need to be informed about the trial as soon as feasible after the intervention has been given.

   Subjects targeted under 21 CFR 50.24 require additional protections of their rights and welfare and will be considered vulnerable subjects for purposes of Legacy IRB review.

207. Planned number of subjects. The planned enrollment of subjects at the site must be consistent with the protocol submitted for review. Discrepancy in planned site enrollment and protocol inclusion/exclusion criteria cannot be approved unless the PI provides the specific rationale for deviation from the protocol to be approved. Allowable deviations from the protocol may include a lesser number of planned subjects for the site, a request not to allow consent by a legally authorized representative (LAR) where the site chooses to only allow subjects that can consent for themselves, or requests to enroll subjects not specifically mentioned in the protocol but not excluded from the research e.g., employees. All deviations from the protocol description of the planned population must be approved by the IRB.

208. Consistency among protocol and other documents. The information in the research consent form should be consistent with the protocol and should provide some information about the population under study. The number of subjects to be enrolled at the site should be communicated in the consent form but is not required. Changes in the number of subjects to be enrolled at a local site of a multicenter study are not considered to be modifications to previously approved research when the number of subjects to be enrolled in the entire study is unchanged.

209. Compensation of Subjects for Participation. Regulations provide no clear guidance on the level of compensation that should be offered to research subjects. Regulations state that researchers seek consent only under circumstances that minimize the possibility of coercion or undue influence (45 CFR 46.116). Research incentives may limit the ability of the research

subject to provide truly voluntary, informed consent. Subjects should be able to make informed decisions to participate based on the real risks and benefits of participation, but not on compensation. Subject compensation should be equitable, and the confidentiality of information related to payments should be protected. See for example, https://cphs.berkeley.edu/compensation.pdf

210. Compensation Types: Subjects can be paid or given non-monetary rewards as remuneration for time and participation and as incentives to participate. Compensation can be cash, gift cards, vouchers, reimbursement for costs, etc.

211. Problems with compensation. Problematic compensation might include "undue influence," when the offer of an excessive or inappropriate reward is made to obtain compliance, or "coercion," when an overt or implicit threat of harm or negative consequences is intentionally presented by one person to another in order to obtain compliance.

212. The plan for compensation to subjects should be detailed. PIs should fully describe the plan for compensation of subjects and the amount, method, and terms of compensation. The informed consent document should disclose all information concerning payment, including the total amount, schedule/form of payment, and any plans for prorating payment if a subject withdraws.

213. Compensation is not considered a benefit under the criteria for approval and is not considered when the IRB weighs the risks and benefits of the research. Compensation is an incentive or payment only, not a benefit of the research.

DOMAIN 3: RESEARCH SITE(S) FOR THIS STUDY

301. IRB approval of the research includes the specific site(s) of the research
302. The PI must have the ability and privileges to conduct research at Legacy
303. The site(s) of the research must be provided
304. The list of Legacy sites is non-exhaustive
305. Legacy sites not engaged in research
306. The PI must have permission to conduct research at Legacy
307. The PI must provide assurances that all Legacy policies will be followed
308. Location of consent of subjects
309. Adequate site for the conduct of the research
310. Subject privacy and confidentiality at the research site
311. Incidental Medical Care at Legacy
312. Adding new site
313. Site visits

301. **Approval of research requires approval of the site of the research.** Approval of research at Legacy includes approval of the PI and of the specific site(s) of the research at Legacy. The PI must provide information about their role at Legacy, the department the PI is employed in, and the site(s) where the research will take place. If site(s) information changes during the study, the PI must notify Legacy IRB and request approval of the new site(s). If the research is approved before the research site(s) is known, the research may be approved contingent on site(s) being identified later and submitted to the IRB for approval.

302. **PI's role and position at Legacy must be specified.** The PI's position at Legacy must be consistent with their ability and privileges to conduct research at Legacy. The PI must provide information about their active role at Legacy as a physician, RN, other medical personnel, and/or as an employee or contractor, a medical professional with staff privileges, etc.

303. **The site (s) of the research must be provided.** The PI must indicate the site(s) where the research will take place. This includes all departments where specific research procedures will take place (but does not need to include departments where standard care procedures will be done). The PI must confirm that subjects will only be consented by listed and approved Legacy study staff or other non-Legacy staff that have been approved for the research and their location.

304. **Legacy sites by name.** Legacy "sites" include the following non-exhaustive list:

- Legacy Emanuel Medical Center
- Randall Children's Hospital at Emanuel
- Legacy Good Samaritan Medical Center
- Legacy Salmon Creek Medical Center
- Legacy Meridian Park Medical Center
- Legacy Mt. Hood Medical Center
- Legacy Unity Center

- Legacy Silverton
- Legacy Research Institute
- Legacy Investigator's Office or Clinic
- Legacy System Office
- Legacy GoHealth Clinics
- Legacy Devers Eye Institute
- Discoveries in Sight (Devers)
- Legacy Medical Group (all offices)

305. **Legacy sites not engaged in research.** All clinics and partners of Legacy will be considered sites of Legacy unless there are special circumstances to indicate that Legacy Health is not engaged in the research for a particular project because Legacy employees or agents are not obtaining: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

306. **Manager permission to conduct the research.** The PI must have permission to conduct the research from the manager or supervisor of the Legacy department in which the research will be conducted. When requested, The PI must provide documentation of permission from the manager or supervisor of each of the sites and departments in which the research will be conducted. Consequently, the PI must obtain permission from the manager, supervisor, or owner of the site to conduct the research apart from the IRB's review and approval. (If the PI is the owner, manager, or supervisor of the site, the PI should make clear to the IRB that no other approval is needed other than the PI's request.) The IRB will not approve research unless site permission is clear and authority is given.

    Non-Legacy researchers must provide permission from a Legacy manager to conduct the research or partner with a Legacy researcher who has obtained permission. IRB approval of the research does not substitute for departmental manager permission to conduct the research at Legacy. Failure to obtain permission from the relevant Legacy manager for the research to be conducted at the site is a ground for the research to be suspended or terminated and for PI non-compliance to be found by the IRB.

307. **PI Assurances.** The PI must provide assurances that all Legacy institutional policies will be followed during the conduct of the research.

308. **Location of consent of subjects.** PI and location of consent of subjects is required. The PI must indicate the site(s) where the PI is primarily located and where subjects will be seen, recruited, and consented and who will conduct the consent process.

309. **Adequate site for conduct of the research.** The site must be adequate and safe for the research procedures. The site must be adequate for subject safety and welfare consistent with the medical procedures planned for the research.

310. **Subject privacy and confidentiality at the research site.** The PI must provide assurances to the IRB that site(s) provide adequate privacy and confidentiality to enroll, consent, and

conduct subject procedures at the site(s). The site must ensure that it will provide privacy and confidentiality to subjects in research consistent with standard clinical practice or standard research protections.

311. **Medical Care at the site.** Incidental medical care of a research subject does not trigger a need to add a Legacy research site. Incidental care at Legacy of a research subject at a distant site does not make Legacy a research site, nor Legacy staff researchers, nor is informed consent required to treat. *See "Use of Investigational Products When Subjects Enter a Second Institution, Guidance for Institutional Review Boards and Clinical Investigators,* JANUARY 1998. http://www.fda.gov/RegulatoryInformation/Guidances/ucm126432.htm

312. **Adding new sites.** The addition of a site to a previously approved study is considered a modification to previously approved research. If additional sites are added to the research study that were not previously approved by the IRB, a change in research should be submitted for review and approval.

313. **Site Visits.** The IRB may require an IRB site visit by an IRB-authorized visitor to a site where Legacy has oversight. The purpose of the site visit may include the following reasons:

- Observation of the consent process
- The IRB wants verification from sources other than the investigator that no material changes have taken place since the IRB review.
- There are allegations or findings of non-compliance.
- The nature of the research indicates that the consent process can be improved through observation.
- There are concerns raised regarding the scientific integrity of the research to be reviewed.
- There are concerns raised regarding the scientific integrity of the PI to be reviewed.

The IRB or IO will determine who conducts the site visit and observation. The IRB may have the observation conducted by: IRB office staff, IRB members, or an independent person appointed by the IRB,

The site visitor may observe an actual consent process and determine whether the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally authorized representative, and that informed consent was freely given by the participant or the legally authorized representative. The site visitor may review the records of subjects that have consented or been screened or enrolled in the research overseen by the IRB.

DOMAIN 4: JURISDICTION AND SPONSOR(S)/FUNDER(S) OF THE RESEARCH

401. Sponsor
402. Sponsor-Investigator
403. Funder
404. COI of PI, Sponsor, Funder, Institution
405. Federally Funded
406. Single IRB Requirements
407. Central IRB Requests
408. Responsibilities of Central and Ceding IRBs
409. Review of Request to Waive or Cede Authority to Central IRB
410. Review and Waiver of minimal risk or exempt research to another IRB Review
411. Oversight of the research by a PI
412. Sponsor responsibilities
413. Agency jurisdiction
414. Data Protection Plan
415. Statement of Compliance
416. Exempt research
417. Oregon/Washington law

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401. Sponsor. The PI must indicate whether there is a sponsor and/or a funder of the research. A "sponsor" is defined as a person or organization who takes responsibility for and initiates a research project of clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor is defined and limited by their ability to direct or regulate the conduct of the PI in the research. When requested, the PI should clearly describe when an organization is or is not taking the role of the sponsor and clarify any ambiguities regarding a sponsor's role in the research.

402. Sponsor-Investigator. The sponsor does not usually conduct the investigation unless the sponsor is a sponsor-investigator. A sponsor-investigator is a PI that initiates and conducts their own research.

403. Funder. The "funder" of the research is the entity providing financial support for the study. The funder may or may not be the sponsor of the research. The funder may be external or internal to Legacy or the PI or a Legacy department may be self-funding the study. The IRB must be provided funder information to adequately assess whether a conflict of interest may be present in the study.

404. Conflicts of Interest of the PI, Sponsor, Funder, or Institution. When requested, the PI must submit information about the sponsor, funder, or institutional conflicts of interest (COI). A COI of a sponsor, funder, or institution may include a monetary value not limited to salary or other payments for services (e.g., consulting fees or honoraria), equity interests (e.g. stocks options or other ownership interests), and intellectual property rights

that exceed $5,000 per annum if salary, fees or other continuing payments represent more than a 5 % ownership for any one enterprise.

PIs must also report any financial benefits made available in connection with the conduct of a study that are in addition to the ordinary compensation for services beyond customary and reasonable fees, including incentive pay, rewards for early recruitment, or bonuses for reaching enrollment goals. Institutional COIs may include intellectual property ownership, tech transfer interests, etc.

Where the PI indicates a sponsor, funder, or institutional COI, the Legacy IRB is tasked with determining what action should be taken to manage that conflict. These actions may include but are not limited to:

- public disclosure of the conflict through inclusion in the consent form or other subject documents
- monitoring of the research project by independent reviewers
- modification of the research plan
- disqualification of the investigator, sponsor, funder, or institution from participating in all or a portion of the research
- elimination of any financial interest in any research sponsor, funder, or institution

405. Federally Funded Research. Federally funded research triggers several regulatory requirements. For one, the federal regulations under 45 CFR 46 must be applied to the research, and for each federal agency funding the research, there may be additional regulatory requirements. If a study is federally funded (in whole or part), the PI must indicate and list which agency is supplying that funding, e.g. NIH, NSF, DoD, EPA, etc. The regulatory requirements for different agencies apply, and the IRB may need to make special findings related to the proposed research.

406. Single IRB Requirements. Federally funded research may require a single IRB (sIRB) for the study, even where a Legacy PI, site, and patients would typically require review by Legacy IRB. In the conduct of cooperative research projects, each institution (or entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable regulations. However, sIRB mandates that local IRBs cede or waive oversight to an external IRB if the institution wants to participate in or conduct the proposed research at their site. The Legacy Research Institute (LRI) VP of Research, acting in their capacity as IO, determines whether Legacy will cede or waive IRB oversight to an external IRB for sIRB requirements. The determination about whether to cede or waive oversight to an External or sIRB is made by the IO with advice from the IRB Administrator and IRB members. The IO may choose to refer the project to the Legacy IRB for consideration of the waiver request and to advise them while making the decision to cede or waive. Legacy Health IRB is not obliged to cede or waive any study to an external IRB, whether sIRB (for a federally funded study) or a central IRB. The IO reserves the right to decline any request for deferral to another IRB.

407. Central IRB Requests: A request for an IRB to cede or waive to an external or central IRB is similar to but not the same as a sIRB mandate request. In the conduct of

cooperative research projects, each institution (or entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable regulations. Federal regulations allow for cooperative research projects which involve more than one institution. To avoid duplication of review efforts by IRBs, the IO can choose to conduct joint reviews or rely upon the review of an external or central IRB. The determination about whether to cede or waive oversight to an External or sIRB is made by the IO with advice from the IRB Administrator and IRB members. The IO may choose to refer the project to the Legacy IRB for consideration of the waiver request and to advise them while making the decision to cede or waive. All research that utilizes Legacy sites, Legacy patients, or Legacy employees is presumed to come under the jurisdiction of Legacy IRB oversight, and Legacy Health IRB is not obliged to cede or waive any study to an external IRB or a central IRB. The IO reserves the right to decline any request for deferral to another IRB.

408a. Responsibilities of the External or Central IRB:

1. Perform initial reviews and decide to approve or disapprove the study.
2. Maintain and make accessible to the Legacy IRB the initial protocol, protocol reviews, approvals and disapprovals and minutes of IRB meetings.
3. Carry out Continuing Reviews, reviews of Serious Adverse Events, reviews of protocol amendments, and reviews of DSMB reports. These documents will be maintained and made accessible to the Legacy IRB.
4. Maintain an IRB that satisfies the requirements of the Common Rule and provide special expertise as needed from IRB members or consultants to adequately access all aspects of each study.
5. Make available the roster of the External or Central IRB membership as well as the Standard Operating Procedures and Policies.
6. Notify the Legacy IRB of any suspension or restriction of study activities.
7. Provide a final report to the Legacy IRB upon the completion of the study.

408b. Responsibilities of the Legacy IRB

1. Ensure the safe and appropriate performance of the research at its institution. This includes but is not limited to, monitoring study compliance, major protocol violations, and any serious adverse events. Provide a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified should be promptly communicated to the External or Central IRB.
2. Require that investigators and other staff at Legacy who are conducting the research are appropriately qualified and meet Legacy's standards for eligibility to conduct research.
3. Notify the External or Central IRB if there is a suspension or restriction of the local investigator.
4. Provide the External or Central IRB with the name and address of the local contact person, such as the IRB administrator.

5. Establish a procedure by which the local IRB receives and reviews the External or Central IRB's materials for studies to be performed at Legacy. This includes reviewing the External or Central IRB's materials, determining if there are any local concerns, determining whether the review is acceptable to the Legacy IRB, and deciding whether to accept the External or Central IRB's review.
6. As appropriate, add local language to consent forms approved by the External or Central IRB, including the Legacy Liability Statement, reference to Legacy regarding consequences of the research subject's voluntary withdrawal from the study, and include contact local information concerning who to ask regarding the rights of the research subjects.
7. If Legacy accepts the review of the External or central IRB, the Legacy IRB will maintain records and evidence regarding the study's approval, continuation, and closure.
8. Maintain a local IRB whose membership satisfies the Common Rule.
9. Maintain a human subjects protection program as required by DHHS' Office for Human Research Protection.
10. Ensure that local IRB members and local investigators receive initial and continuing education on the requirements of human subjects protection.
11. Maintain a Federal Wide Assurance and designate the External and Central IRB's authorization through an appropriately executed agreement.

409. Review of Request to Waive or Cede Authority to Central IRB. Legacy Research Institute (LRI) VP of Research determines whether Legacy cedes or waives IRB oversight to an external IRB for sIRB requirements. The determination about whether or not to cede or waive oversight to an external or sIRB is made initially by the Institutional Official with advice from the IRB Administrator. The IO may choose to refer the project to the Legacy IRB for consideration of the waiver.

410. Review and Waiver of minimal risk or exempt research to another IRB Review. The Legacy IRB Research Regulatory Specialist may determine whether a clearly minimal-risk research proposal may be ceded to an external IRB. If the proposal is unclear on whether the proposal is minimal risk, the Research Regulatory Specialist may request the IO's input or schedule for full board IRB review. Proposals with especially sensitive or vulnerable populations or other special issues should be scheduled for full IRB review. Examples: CARES data, Legacy employee research that implicates performance, special categories of patients such as sex abuse victims, patients with mental health concerns, patients with legal problems, etc.

411. Oversight of the research by a PI. The PI must indicate who is overseeing the research in all respects and must specify whether the PI is the sole investigator, Co-Investigator, or a sponsor-investigator. The PI is required to indicate if there are additional parties or stakeholders to the research and to specify their role in the research.

412. Sponsor responsibilities. There are specific responsibilities the study sponsor is required to fulfill. The sponsor is responsible for choosing "qualified investigators", "ensuring proper monitoring of the investigation," and "ensuring that the FDA and all participating

investigators are promptly informed of significant new adverse events or risks"; that any transfer of responsibilities is done appropriately, and that investigators and monitors who are chosen are qualified by training and experience and who commit to upholding all required responsibilities.

413. **Agency jurisdiction.** The study submission is required to provide enough information to determine what legal agencies have jurisdiction over the research. The PI should indicate whether the study falls under FDA regulations (for a device or drug or biologic study), or whether PHI information is implicated, triggering oversight by the Office of Civil Rights (OCR), or whether Oregon law applies e.g., the age of majority for minors, or when mandatory reporting is required, etc. Federal funding will trigger the oversight of the Office of Human Research Protection (OHRP). The PI is also required to comply with all Legacy policies and procedures and is tasked with understanding that some research procedures may trigger Legacy standard policies and procedures. The PI is required to abide by all legal requirements as noted by the IRB.

414. **Data Protection Plan.** Data from Legacy patients require a data protection plan regardless of how anonymized or de-identified the data is rendered under the research. The PI must indicate in the study submission how Legacy patient data and PHI will be protected and not disseminated beyond the stakeholders in the research. The PI must specify all data to be disseminated, how it will be shared, and who it will be shared with beyond Legacy.

415. **Statement of Compliance**: The Legacy Institutional Review Board (IRB) is authorized and responsible for the review and approval of all research involving human subjects that utilize Legacy Health facilities, clinics, resources or patients, and affiliated sites or partners. The IRB is a federally mandated board charged with protecting the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable Legacy Health policies and federal and state regulations.

The Legacy IRB is governed by an assurance granted by the Office of Human Research Protections (Federal Wide Assurance #00001280).

In addition to that assurance, the Legacy IRB is governed by Legacy Health institutional policy (LHS 100.18) and is in compliance with local regulations and the regulations of the US FDA as described in 21 CFR Parts 50 and 56, and the United States Department of Health and Human Services 45 CFR Part 46.

Legacy Health is registered with the Office for Human Research Protections (OHRP) and FDA as IRB0000398.

Legacy IRB is registered with the State of Oregon per ORS 192.547 (genetic privacy).

There are two IRB committees at Legacy Health, one that meets at Good Samaritan Hospital and one at Emanuel Hospital. Both committees can review studies that are based

at any Legacy-associated facility. Legacy IRB Committee #1 is registered with DHHS under IRB00000677. Legacy IRB Committee #2 is registered with DHHS under IRB00000678.

416. **Exempt research.** Research determined to be exempt from Legacy IRB oversight must be determined by the Legacy IRB Administrator or IRB staff. Research that falls outside of the oversight of the common rule or is deemed not to be human subjects research is determined by the Legacy IRB.

417. **Oregon/Washington law.** Legacy jurisdiction of research not subject to FDA or OHRP jurisdiction will be governed by Oregon and Washington State Law, and Legacy policies and procedures.

DOMAIN 5: RESEARCH TYPE

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501. Identification of Type of Research. The PI must identify the research type that is proposed for IRB review and approval. Diverse research types or designs will trigger diverse regulatory requirements and ethical considerations that must be resolved for approval to be granted. The PI is required to provide information that clarifies the IRB's concerns regarding research type, design, and procedures. Under no circumstance will the IRB abdicate the responsibility to ensure that the research type and design are consistent with sound research design according to current scientific standards, have an adequate risk/benefit ratio, and ensure additional protections for vulnerable subjects.

502. FDA Studies. Proposed studies under FDA jurisdiction must be identified so that all regulatory requirements are applied to the research. Regulatory requirements and adequate documentation for review of devices, drugs, and biologics must be submitted for approval, including investigational new drug designation (IND #), investigational device exemption (unredacted IDE documentation), non-significant (NSR) risk claims, IND exemption claims, etc. Research consent forms for FDA research must contain all FDA-required language and elements.

503. Federally funded research. Federally funded research must be identified so that all regulatory requirements under 45 CFR 46 are applied. Research consent forms for federally funded research must contain all 45 CFR 46 required language and elements.

504. Ethical Analysis of Research. Ethical concerns in research are triggered by the use of poor study design, randomization, enrollments of vulnerable populations, use of placebos or sham surgery, use of investigation or experimental test articles, a disparity in providing standard care to vulnerable populations, unequal or unfair subject selection, inappropriate waiver of informed consent, or diminished or inadequate informed consent, undue influence in recruiting or enrolling subjects, exploitation, unprotected collection of data regarding subject illegality or stigma, conflicts of interest, therapeutic misconception, and use of surrogates for the consent of subjects, etc. For approval, the PI must provide justification and documentation supporting any procedures or processes in research that trigger ethical concerns, as many of the typical ethical concerns do

not have clear regulatory requirements, and the IRB must determine the approval of the research by general requirements in the criteria of approval.

505. Criteria for approval of research. The IRB must apply the criteria for approval to all research under 45 CFR 46.111 for federally funded research and for FDA research under 21 CFR 56.111.

506. Sound research design. To be approved, the IRB must ensure that the proposed research meets the elements of "sound research design" under 45 CFR 46.111 and 21 CFR 56.111. The protocol should outline the type of research and should provide enough information to ensure 1) that the number of subjects to be enrolled will be enough to support the "sound research design" proposed, 2) that the design of the study does not unnecessarily expose subjects to risks, 3) that the design will, at minimum, advance knowledge, or will, if possible, provide benefit to subjects, 4) that the risk/benefit ratio is reasonable, 5) that vulnerable subjects are protected, 6) that subjects have consented where necessary, and 7) the study data is monitored for safety.

507. Risks must be described. The risks of the research must be detailed in the protocol and/or the consent form, and the IRB should make relevant risk findings: minimal risk, greater than minimal risk, a minor increase over minimal risk, or other risk findings as appropriate. Specific risk findings are required for research involving children, prisoners, and pregnant women and their fetuses.

508. Expert review is available. The convened IRB (or expedited reviewer) has, or has obtained through consultation, adequate expertise to review the research. The IRB (or expedited reviewer) shall have the discretion to require the PI to obtain additional expertise to inform the IRB of the nature of the research as needed.

509. Adequate resources. The research has the resources necessary to protect subjects. The resources to conduct the research properly should include the time to conduct and complete the research, adequate facilities for the safety and welfare of the subjects, an adequate plan to recruit subjects and medical/psychosocial resources, qualified investigators, and adequate research staff.

510. Grant funding consistency. The research should be consistent with the grant funding. The IRB has a right to require the submission of the grant funding application to ensure that the protocol is consistent with the grant.

511. Quality improvement determination. Some Quality Improvement (QI), Exempt research, Case studies, Student or Fellows research, or research determined to not be human subjects research do not necessarily fall under the jurisdiction of Legacy IRB. However, all such findings or determinations of research are made by the Legacy IRB Administrator or designee. Legacy Health requires that all research projects be reviewed by the Legacy IRB to ensure that the research does not fall under IRB jurisdiction.

512. Common Types of Research. The following list of common research types is non-exhaustive:

- Clinical Trials: Phase I-IV Drug Trial
- Drug
- IND
- Vaccine
- Biologic
- Exempt Drug
- Device Trial
- IDE
- NSR Device
- Exempt Device
- Assay Device
- HUD/HDE
- Treatment/Compassionate Use/Emergency Use: use of investigational drug or device for one patient
- Emergency research/FDA under 21 CFR 50.24 -- Exception from Informed Consent (EFIC)
- Cancer Treatment
- Oncology
- Radiation
- Randomization
- Blinded
- Double-blinded
- Placebo
- Sham Device
- Tissue/Specimen for future research
- Tissue/Specimen Banking
- Genetic Information
- Genome-Wide Association Study (GWAS)
- Social-Behavioral
- Behavioral -- Randomized Controlled Trial
- Survey/Interview
- Focus Group
- Observational
- Deception (waiver of the purpose of research)
- Illegality/Stigma: e.g., embarrassing or criminal behavior
- Outcomes Research
- Quality Improvement/Program Improvement
- Health Policy Trial (trials innovation in the delivery of services for patients or providers)
- Usability or “look and feel”
- Pilot/Feasibility (preliminary research on a small number of subjects)
- Multi-Site (addition of sites to a previously approved study protocol)
- “Big Data” (study using a large volume of patient or confidential data)
- Case study (workup of 1-2 patients; not intended to be generalizable)
- Pragmatic Clinical Trials (trials designed to test the effectiveness of multiple standard-of-care interventions in a broad routine clinical practice)
- Registry/Prospective Data Gathering
- Retrospective Chart Review

DOMAIN 6: RESEARCH RISKS AND PROCEDURES

601. PI knowledge of the Risks, Benefits, and Procedures of the Research
602. Research Risk and Investigational Treatments
603. Drug Studies
604. Device Studies
605. The risks and procedures of the research must be described
606. The benefits of the research must be described in the protocol and in the consent form
607. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research
608. The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as research risks.

601. PI knowledge of the Study. The PI will be able to answer questions about the risks, benefits, and procedures of the proposed research and will be available to the subjects to answer questions about the study.

602. Research Risk and Investigational Treatments. The research must identify the following non-exhaustive elements as relevant to the risks of the research:

- Pilot/Feasibility: research on a small number of subjects intended to gather data only for future research.
- Intervention via test articles or therapies or subjects being randomized to various study arms.
- Blinded or double-blinded study.
- Placebo or Sham surgery controlled.
- Research enrolling vulnerable populations: Children/Minors, Pregnant Women/Fetus,
- Prisoners, Legacy Employees, Students, Transgender, Poor, Uninsured, Non-readers, Sensitive populations (stigmatized, marginalized, minority), subjects requiring surrogate consent, unconscious or subjects with cognitive impairment.
- "Big Data" study using a large volume of confidential or HIPAA-protected patient data.
- Use of data normally protected by standard medical privacy or confidentiality, a breach of which could cause embarrassment or reputational harm to a subject.
- Whether the research involves investigational (experimental) treatments.
- Whether the research involves departure from standard clinical care procedures.
- Whether the research is greater than minimal risk because the probability and magnitude of harms or discomforts anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- Whether consent form clearly describes all specific physical, psychological, social, economic, or other risks to the subjects, including the nature of risks, the seriousness of risks, and incidence or probability of the risks.
- Whether the study requires special credentialing and training for study staff and whether such training has been obtained by the PI and/or relevant study staff, and documentation of such credentialing is or will be available upon request prior to initiation of the study.
- Whether a Data Safety and Monitoring Board (DMSB) be used.

- Whether a Medical Monitor be utilized.

603. Drug Studies. For Drug studies, the following information must be indicated where relevant:

- IND Study: The drug has an IND, and the study may pose greater than minimal risks to subjects. Adequate documentation is available from the sponsor, indicating that the IND # has been obtained and that the study may begin. Required FDA documentation must be submitted or available.

- The study meets the criteria for an IND Exempt Study (package insert or other documentation is required):

    - The clinical investigation of a drug product that is lawfully marketed in the United States is exempt from the requirements of this part if all the following apply:
    - The investigation is not intended to be reported to the FDA as a well-controlled study supporting a new indication for use or to support any other significant change in the drug's labeling.
    - If the drug under investigation is lawfully marketed as a prescription drug, the investigation is not intended to support a significant change in the product's advertising.
    - The investigation does not involve a route of administration, dosage level, use in a patient population, or another factor that significantly increases the risks (or decrease the acceptability of the risks) associated with the use of the drug product.
    - The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in part 50, and
    - The investigation is conducted in compliance with the requirements of Sec. 312.7 (Promotion of investigational drugs)

- On-Label Study (package insert or other documentation is required): The drug is being used on-label and not investigational in any way.

- Dietary Supplement Study: An herb or dietary supplement be used for investigational purposes.

- Placebo-controlled study: Some subjects in this drug study will receive a study drug that contains a placebo.

- Other Drug Study: The drug being used in the study is being used for treatment purposes only.

604: Device Studies. For Device studies, the following information must be indicated where relevant:

- Non-Significant Risk (NSR) Study: The PI or sponsor considers the use of this device in the study to meet the criteria for a Non-Significant Risk (NSR) study. The protocol or a separate statement is submitted showing how this study meets the criteria for an NSR Study. Note: an NSR study is not equivalent to a minimal-risk study. Documentation must be submitted.

- Significant Risk (SR) Study: The device has an IDE#, and the study may pose significant risks to subjects. Therefore, the study is greater than minimal risk. Required FDA documentation must be submitted for review.

- 510(k) Device Study: The device has a 510(k) approval, and it is being used and studied according to its approved indication. Documentation must be submitted.

- PMA Device Study: The device has PMA approval and is being used and studied according to its approved indication. The required FDA documentation must be submitted.

- Diagnostic Device Study: The device is a diagnostic device, and in this clinical investigation, the testing is 1) noninvasive, 2) does not require an invasive sampling procedure that presents significant risk, 3) does not by design or intention introduce energy into a subject, 4) is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. Documentation must be submitted.

- Device Usability Study: The device is being studied for consumer preference or usability testing only, and a) the testing is not for the purpose of determining safety or effectiveness. Documentation must be submitted.

- HUD Use: The device is a Humanitarian Use Device (HUD) with HDE #; it is not being used investigationally but per its HUD approval. Documentation must be submitted.

- HUD Study: The device is a Humanitarian Use Device (HUD) with HDE #. It is being studied for safety and efficacy to obtain pre-market approval within the approved labeling. Documentation must be submitted. Because this is research, subjects will be consented to via a research consent form.

- HUD Study (new use): The device is a Humanitarian Use Device (HUD) and has HDE #, but it is being researched for a new use outside the approved labeling. Thus, the IDE regulations must be followed. Required FDA documentation must be submitted for review.

- Other Device Study: The device being used in the study is being used for treatment purposes only.

605. The PI must indicate the risks and procedures of the research in both the protocol and the consent form. All documentation regarding research risks and research procedures must be consistent and clear. The IRB may require that risks and procedures set out in the protocol and consent form be revised to ensure clarity for both study staff and subjects that revisions are made to clarify the frequency or rarity of risks, or that risks and procedures be presented in a way that is more understandable to subjects.

606. The PI should specifically indicate the benefits of the research in the protocol and must indicate the benefits of the research in the consent form. The study must indicate the anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result, however small. The consent form must inform the subject that there may or may not be a direct benefit to the subject and, if no direct benefit, that the benefit of the research may be knowledge creation only.

607. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). To adequately assess the research, the focus of the IRB of the research is and should be on the research risks, benefits and procedures of the proposed research. Where the research is departing from standard clinical care, treatment, or practice, for subjects (of any cohort of subjects), the IRB should evaluate whether the departure from standard care itself raises unacceptable risks to subjects, even where the research risks from such departure is minimal or low risk.

608. The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility. While the IRB is tasked to consider the "importance of the knowledge that may reasonably be expected to result" from the research in the context of determining the risk/benefit ratio of the proposed research, the regulations also specifically caution that the IRB should not consider the ultimate or long-term effects or risks of the knowledge to be gained from the research, apart from the direct risks, benefits, and procedures to the subjects to be enrolled into the research.

DOMAIN 7: CONSENT PROCESS AND FORM

Sections 701 – 708 are not used
709. Consent Form Stamp
710. Consent Form Signatures
711. Date and Time of Consent
712. Remote Consent
713. Surrogate Consent
714. Remote Surrogate Consent
715. Remote Consent for Minimal Risk Studies
716. Re-Consent of Subjects via Communication of New or Updated Study Information
717. Use of Screening Consent Forms
718. Recruitment/Receptionist Scripts
719. Key Summary
720. Non-English-Speaking Subjects
721. Advertising and other subject materials
722. Doctor to Doctor communications
723. Waiver of elements of informed consent
724. Deception
725. Waiver of Documentation of informed consent

709. Consent Form Stamp. The IRB-approved consent form will be stamped showing the date of approval unless regulatory partners, investigators, or sponsors request an un-stamped consent form with other acceptable methods of version control. The stamp is placed to signify the approved text and is to be retained by the investigator. In some cases, investigators have used a copy of that stamped consent form to present to research subjects. The PI should only use the most recently approved consent form for enrolling subjects.

710. Consent Form Signatures. The consent document is a written summary of the information that should be provided to the subject. Many clinical investigators use the consent document as a guide for a verbal explanation of the study. The subject's signature provides documentation of agreement to participate in the study.

a. The following signatures **must** be affixed to the consent form and dated:

- signature of the research subject
- signature of the principal investigator or their designee who is conducting the consent session

b. The following signatures **may** be affixed to the consent form and dated:

- signature of the witness (someone not involved in the study, the witness must be present during the entire consent process)
- signature of a parent or legal guardian
- signature of next of kin (if research subject is not cognitively competent to consent); next of kin is defined as being spouses, 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 equivalent to a family relationship.

711. Date and Time of Consent. Each signature line must include a place to note the date, but the time of consent is not required. The investigator or the sponsor may request capturing the time the consent is collected. Noting the time of consent provides an indicator that consent was obtained in a manner that allowed the subject sufficient time to consider the risks, benefits, and alternatives.

712. Remote Consenting. A consent session conducted over the telephone, or some other form of technology is not the same as consent for treatment trials that require and would insist on a face-to-face consent process.

However, technological changes and the need for remote consent now make it more likely that consent will be captured via phones, computers, etc. The FDA allows flexibility for remote consenting. Remote consent may proceed where there is a good reason consent cannot be obtained in person. For example, this might be appropriate if the potential subject lives in another state and the study site wants to screen the individual to determine their eligibility for the study before the individual spends a lot of money or time traveling to the study site. In such a situation, the FDA would expect the consent form to be emailed or faxed to the subject or their legally authorized representative (LAR), discussed by phone, signed and dated by the subject, and scanned and emailed or faxed back to the PI. The purpose is to provide the subject and/or the LAR with an opportunity to discuss the information in the consent form and have their questions answered prior to the subject's enrollment in the study. The consent process must otherwise be the same as if the subject was at the site, they have the consent form, they can ask questions of the PI, they can wait and discuss with family, etc. They sign and date it and mail, scan and email it, or fax it back to the PI/site.

A remote consent process is not a “waiver” of consent or of any required elements of consent, nor is it a form of truncated or shortened consent. It is an alternative method of informed consent that is consistent with regulatory requirements.

713. Surrogate Consent. If a prospective subject cannot consent on their own behalf, federal regulations permit researchers to obtain consent from a legally authorized representative (LAR). For researchers to obtain consent from a subject’s LAR, the IRB must approve the use of surrogate consent consistent with State law. The IRB should be cautious about a request to allow an LAR where the study is greater than minimal risk, is inconsistent with minimal risk, or does not provide a prospect of direct benefit to the subject being enrolled in the research. Individuals whose medical condition may render them temporarily unable to provide informed consent because of severe pain, confusion, or impaired consciousness due to events such as life-threatening illness or trauma, and individuals who have cognitive impairments such as intellectual disabilities, dementia, or psychosis that are enduring or that may worsen with time. Those individuals who may grant surrogate consent include:

- a person’s agent designated by an advance health care directive

- a conservator or guardian of the person having the authority to make health care decisions for the person
- spouse of the person
- domestic partner of the person
- adult son or daughter of the person
- the custodial parent of the person
- any adult brother or sister of the person
- any adult grandchild of the person
- an available adult relative with the closest degree of kinship to the person.

If surrogate consent is sought, the PI or their staff will document the circumstances under which it was obtained (or not) and the surrogate's relationship to the subject.

714. Remote Surrogate Consent. In some studies where the patient is not conscious or cognitively impaired, or for any other reason unable to provide informed consent, it is acceptable to send the informed consent document to the legally authorized representative by FAX, email, or mail and conduct the consent interview by telephone or videoconference when the representative can read the consent as it is discussed. If the legally authorized representative agrees, they can sign the consent and return the signed document to the clinical investigator by FAX or email, etc. prior to initiation of the experimental treatment.

715. Remote Consent for Minimal Risk Studies. Studies that involve surveys, interviews, or other minimal risk studies may, in some instances, qualify for a waiver of the usual requirement of written signed consent. In those instances, a script must be submitted by the PI to the IRB and approved in place of a consent form.

716. Re-Consent of Subjects via Communication of New or Updated Study Information. Changes in the study and/or consent form that occur after a research subject has already consented to be in the study that need to be brought to the attention of the research subject generally concern:

- Update on risks
- Changes in procedures, including additional procedures
- Changes to the duration of subject involvement
- Changes/added visits
- Changes to payments or compensation

Updates to risk assessments should be communicated immediately through a phone call or letter to the subject or both, and then at the next clinic visit, that information should be presented in the form of a consent addendum or updated consent form or any method that adequately apprises the subject of the new information. The updated consent form or addendum should be limited to just the new risks that have emerged during the study. A signature of the participant and the researcher on the updated consent form or addendum is required to document that the research subject has been made aware of the updated risk assessment. Consent addendums, letters and memos to subjects, and phone scripts communicating such changes must be reviewed and approved by the IRB.

717. Use of Screening Consent Form. In those instances where patients go through extensive screening processes prior to enrollment, a screening consent form can be used. That consent form will describe the main study briefly and concentrate on the purpose, procedures, and risks of the screening processes. A screening consent form is intended for those studies where it is anticipated that there will be a high number of screen failures and/or involve procedures that pose a risk to the subject. Screening consent forms must be reviewed and approved by the IRB.

718. Recruitment/Receptionist Scripts. The first contact study subjects make is often with a receptionist/recruitment staff who follows a script to determine basic eligibility. In some cases, personal and sensitive information is gathered about the individual. The IRB should ensure that the procedures adequately protect the rights and welfare of the research subject. Issues for IRB review of scripts include: what happens to personal information solicited during the phone conversation? Are names collected and then used for another study? Receptionist scripts are considered part of the consent process and must be reviewed and approved by the IRB.

719. Key Summary. For federally funded studies, a "key summary" is required for research informed consent forms, which are very complicated. The key summary is information about the study presented in brief form as the initial pages to the full consent form to help the subject or LAR decide whether they want to consider participation in the study. The key summary must contain a brief summary of the purpose of the study, the activities of participation and the risks.

720. Non-English-Speaking Subjects. In some cases, individuals who do not speak English as their primary language and who have limited ability to read, speak, write, and understand English may directly benefit from enrollment in a clinical research study. Such individuals may ask or be asked to participate in a clinical trial in locations where English is the predominant language. The investigators and the IRBs that review such research should carefully consider the ethical ramifications of enrolling or excluding potential subjects when a language barrier may exist between the investigator(s) and some of the potential subjects. Consistent with the requirement that the selection of subjects be equitable, individuals should not routinely be excluded from participating in research simply because they do not understand English.

When non-English speaking individuals are to be enrolled in a study, IRBs and investigators must ensure that the information given to such prospective subjects, or their legally authorized representatives (LAR) is in language understandable to the subjects or their LAR. *Understandable* means the information presented in a language and at a level they can comprehend, including an explanation of scientific and medical terms.

a. Non-English Consent Form Requirements. The IRB must review and approve all English and non-English language versions of any consent documents that investigators use to document subjects' informed consent. The review of the proposed non-English consent forms may be performed at the initial review or as a change in research.

b. Certification of the consent form. The non-English consent forms should be accompanied by a certification that the translation is accurate.

c. Use of interpreters. Informed consent is an ongoing process throughout the course of a subject's involvement in the research. It is required that whenever subjects who do not understand English are involved in research, appropriate interpreter services be made available throughout the course of the research. The investigators should provide the IRB with a description of how interpreters for oral communication will be made available to subjects during the research. For instance, an interpreter will be present throughout the consenting process, including addressing questions by the patient and/or LAR. Additionally, the interpreter may also be present at study visits to address questions throughout the study and the subject's participation.

d. Use of the Short Form. The use of the "short form" for non-English speakers is strongly discouraged. If a PI wishes to use the "short form" in a study, such a procedure must be reviewed by the full IRB.

721. Advertising and other subject materials. The recruitment of research subjects for clinical trials is considered part of the informed consent process. All advertisements that may be seen or heard by a potential research subject must be approved by the IRB prior to its use. IRB review of advertising is necessary to ensure that the information is not misleading to potential subjects.

a. Any communication that is seen or heard by prospective subjects to solicit their participation in a study includes but is not limited to newspapers, TV, radio, bulletin boards, posters, letters, and flyers. The FDA suggests but does not require that the following items should be contained in an advertisement:

- the name and address of the clinical investigator and/or research facility
- the condition under study and/or the purpose of the research
- the criteria that will be used to determine eligibility
- a brief list of participation benefits, if any
- the time or other commitment required of the subjects
- the location of the research and the person or office to contact for further information

b. An advertisement should not contain claims either explicitly or implicitly that the drug or device is safe or effective or that the test article is known to be equivalent or superior to any other drug or device. Advertising should not use terms such as "new treatment," "new medication," or "new drug." Similarly, phrases such as "receive new treatments" or "relieves symptoms" should not be used as they may lead study subjects to believe that they will be receiving newly improved products of proven worth.

722. Doctor to Doctor Communications. Any communication intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor communication (even when soliciting for study subjects), news stories, and publicity intended for audiences, such as financial page advertisements directed toward prospective investors are not considered to advertising and are viewed as professional communication and do not need to be reviewed by the IRB.

723. Waiver of Elements of Informed Consent. Under 45 CFR 46.116(d), the IRB may approve a consent procedure that does not include, or which alters, some or all the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

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

(2) the waiver or alteration will not adversely affect the rights and welfare of the subjects

(3) the research could not practicably be carried out without the waiver or alteration, and

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

The PI must provide adequate information supporting the request to waive consent to meet regulatory requirements under 45 CFR 46.116(d).

As there is no general waiver of informed consent for FDA-regulated research, the use of "deception" in informed consent is limited to non-FDA-regulated research.

724. Deception. Deception in informed consent is a misnomer; the ethical rule is that a partial waiver is accomplished via a waiver of alteration of consent elements, specifically as to the purpose or procedures of the research under 45 CFR 46.116(d).

725. Waiver of Documentation of Informed Consent. A signed consent form is not always required or desired. Under OHRP regulations, per 45 CFR 46.117(c), an IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either:

(1) That the only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern, or

(2) 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.

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

Under the FDA regulations per 21 CFR 56.109(c)(1), the rule is slightly but significantly different. (Note: Section 2 is deleted here, and 21 CFR 50.24 is referenced for additional information for when a waiver of documentation may be obtained under 50.24 research - Exception from informed consent requirements for emergency research.)

An IRB shall require documentation of informed consent in accordance with § 50.27, except as follows:

> The IRB may, for some or all subjects, waive the requirement that the subject, or the subject's legally authorized representative, sign a written consent form if it finds 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 the research context.

In cases where the documentation requirement is waived under paragraph (c)(1) of this section, the IRB may require the investigator to provide subjects with a written statement regarding the research.

DOMAIN 8: PRIVACY PROTECTION AND CONFIDENTIALITY OF DATA

801. Privacy and Confidentiality. To approve research, the IRB shall determine that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data. Possible ethical implications from gathering and disseminating data from subjects include privacy breaches, data ownership and control, data sharing, confidentiality breaches, embarrassment and stigma, transparency, future use, identity, prediction, anonymization/de-identification/masking futility, behavior modifications, discrimination, false interpretations, paucity of legal protections, perpetuity of data collection, IP infringements.

802. Research informed consent requirements. In seeking informed consent, certain information shall be provided to each subject regarding a description of any reasonably foreseeable risks or discomforts to the subject and a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

803. Scope of Protections. Research records include medical information protected by traditional medical privacy laws, HIPAA protections, and research regulations protecting subject privacy and confidentiality.

804. Medical Records. Traditional law protects both the right of an individual to have the medical history of the individual protected from disclosure to persons other than the health care provider and insurer of the individual who needs such information, and the right of an individual to review the medical records of that individual. ORS 192.525(1).

805. HIPAA. HIPAA includes oral, written and electronic forms of confidential medical information. It specifically provides a federal “floor” for protecting patient information and specifically “preempts” state law that is contrary to HIPAA unless an exception is provided.

HIPAA provides that patients have a right to restrict parameters of disclosure, can request amendments to their files, and revoke authorizations for disclosure.

806. Legacy Privacy Notice: LH Privacy notice explicitly informs patients that Legacy may use patient medical information for health care operations and quality improvement, research (that has been approved), be used in de-identified limited data sets for specific projects, provided to business associates, and for public health activities, including research.

807. Protected Health Information: Any information that 1) is received by a health care provider, health plan, or clearinghouse, 2) is transmitted electronically or maintained in any other form or medium (including oral), 3) relates to the provision of or payment for health care for an individual or to the past, present or future physical or mental health condition of an individual, and 4) is individually identifiable. Information is presumed to be de-identified if all the following identifiers have been removed or concealed:

a. patient name
b. street address, zip code, city
c. phone number
d. fax number
e. email address
f. birth date, admission date, discharge date, date of death, all ages over 89
g. social security number
h. medical record number
i. account number
j. health plan beneficiary number
k. certificate/license number
l. vehicle ID number, license plate number
m. device identifier number and serial number
n. Web Universal Resource Locator number
o. Internet Protocol (IP) address
p. fingerprints, voice prints, or another biometric identifier
q. full face photographic images, or
r. any other unique identifying number, characteristic, or code and any associated health information.

808. Data to be collected. For proposed research approval, the PI must identify the type of data to be collected, which may include the following:

- Confidential medical information directly from the subject
- Confidential medical information directly from the subject about the subject's family (e.g. family genetic information)
- Confidential medical record information (e.g., Epic)
- HIPAA or Protected Health Information (PHI)
- Genetic information
- Tissue or bodily fluids to be tested or banked

- Subject (or others) illegality (data, including statements, related to crimes e.g., drug use, firearms, etc.)
- Photographs
- Audio or video recordings
- Notes from interviews, surveys, or focus groups
- Identifying marks or tattoos from the body
- Social media or Internet data e.g., social media information
- Telephone or GPS data
- Genetic Information
- Genome-wide association Study (GWAS) data
- Tissue, blood, or specimen collection
- Sensitive or embarrassing information or data

809. Specimen and Tissue Sample Collection. For proposed research approval, the PI must identify the type of specimens or tissue, if any, to be collected, which may include the following:

- Blood
- Tumor
- Tissues
- Bodily Fluids
- Genetic

810. Future research on data/specimens. For proposed research approval, the PI must identify future research plans for the type of data, specimens, or tissue, if any, to be collected. The plan must specify in detail whether the future research is specified or unspecified:

- Data/Specimens will be banked for further research purposes related to the subject's condition
- Data/Specimens will be used for future research unrelated to the subject's condition
- Data/Specimens will be stored indefinitely for unspecified future use in research
- Data/Specimens will be banked for distribution to other researchers
- Data/Specimens will be stored and made available for research via purchase by third parties
- Data/Specimens to be collected will possibly be used for commercialization purposes
- Data/Specimens to be collected for commercial use and sold to other researchers

811. Commercialization of research data/specimens. The submitted consent form must state how subject data/specimens will be used in the future and/or whether commercialization of subject data/samples is possible or intended. The consent form must advise subjects regarding their rights or lack of rights to profits or benefits from the commercialization of their data/specimens.

812. Access to data. The PI must provide information regarding who has access to the study data for regulatory purposes e.g., the IRB, national coordinating offices, multi-study evaluation centers or sites, pharmaceutical firms, FDA, OHRP, and other government agencies.

813. Protection of data/samples. The PI must provide information regarding how the proposed research will protect study data/specimens by describing whether:

- The data or specimens of subjects will be protected by privacy and confidentiality protections
- Data will be de-identified at a Legacy site before sharing with the sponsor
- The data will be anonymized
- The data Maintained behind a firewall
- The data is only accessed by study staff
- The data is encrypted on a Legacy computer or Legacy laptop computer
- The data is encrypted on a computer outside of Legacy
- The data is secured and locked cabinets
- The data is stored in Redcap or a similar system
- Protected via a Certificate of Confidentiality (CoC) from DHS or Privacy Certificate from DOJ

The data will be subject to data sharing agreements or other business agreements for data sharing data among others.

814. Breach of security plan. The PI must provide information about the plan of action if data security is breached or violated.

815. Storage of data. The PI must indicate how data or specimens of subjects will be stored and protected after the study is complete, which may include the following:

- Data/specimens will be destroyed at the end of the study to ensure subject confidentiality
- Data/specimens will be kept with the PI only at the end of the study to ensure subject confidentiality
- Data/specimens will be kept confidential but will never be used for another research project
- Data/specimens will be kept in storage until the investigational product is approved by the FDA
- Data/specimens will be kept until publication of the results

816. Data analysis. The PI must provide information regarding how the data will be analyzed. The PI must provide information regarding:

- Who the owners of the data are intended to be or will be in the future
- The plans for the publication or presentation of the data
- The plan for Legacy Health acknowledgment as the research site

817. The Consent Form informs subjects of data use and protection. The submitted consent form must adequately and fully inform subjects of the following, if relevant:

- Who will have access to the data collected
- Whether the subject data will be anonymized or de-identified

- What regulatory agencies/bodies will have access to the data
- Whether data/samples will be commercialized
- How data/samples will be used in the future

DOMAIN 9: REVIEW REQUIREMENTS OF THE IRB

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901. IRB pre-review process. Upon receiving a submission for review of research, the following procedure establishes the process to determine the correct process of review:

- Identify missing materials that are needed for an adequate review
- Identify and document the likely determinations or findings that the IRB might need to make in order to approve the research
- Identify relevant local, state, or federal legal issues, if any
- Identify ethical issues, if any
- Identify Legacy Health policy issues, if any
- Determine the likely risk level of the research
- Identify any vulnerable populations by law, e.g., minors, or in fact, e.g., employees
- Determine if there is a need for expert consultation to resolve any identified issues
- Identify other special review issues e.g., conflicts of interests of PI or study staff or sponsor
- Determine the likely level of review – full board, expedited, administrative, exempt, non-engagement, not human subjects research.

Determine whether there is adequate information to satisfy each of the 10 domains of research review:

- DOMAIN 1: QUALIFIED PI AND STUDY STAFF
- DOMAIN 2: SUBJECTS OF THE RESEARCH

- DOMAIN 3: RESEARCH SITE(S) FOR THE STUDY
- DOMAIN 4: JURISDICTION AND SPONSOR(S)/FUNDER(S) OF THE RESEARCH
- DOMAIN 5: RESEARCH TYPE
- DOMAIN 6: RESEARCH RISKS AND PROCEDURES
- DOMAIN 7: CONSENT PROCESS AND CONSENT DOCUMENTATION
- DOMAIN 8: PROTECTION AND CONFIDENTIALITY OF DATA
- DOMAIN 9: REVIEW BY THE IRB
- DOMAIN 10: RESPONSIBLE CONDUCT OF RESEARCH, ETHICS, AND POLICY

After determining that enough information is obtained for review, document the level of review, determine the risks of the study, document the categories of exempt or expedited review, analyze what findings or additional protections are needed for any vulnerable populations, and process the approval or other appropriate board action.

902. Pre-Review of Research. Pre-review by the IRB office is not required and is not to be considered formal IRB action. However, the IRB office may request changes to any submission to ensure that the IRB has the information it needs for formal review and approval of the submission. Requirements to modify, clarify, or revise a submission (or any part thereof) is not a formal IRB action and should not be considered as such.

903. Exempt review by the IRB office. Determinations of exempt research are to be done by the IRB office staff.

904. Expedited Review. IRB staff and designated reviewers appointed by the IO or the Research Regulatory Specialist may conduct expedited reviews of new studies that meet the requirements of approval, changes in research, and other items that may be conducted according to expedited review criteria.

905. Full Board Review. Submissions or items that may not be processed via expedited review or cannot be found to be exempt should be submitted to the full IRB for review.

906. IRB Decisions. The IRB has the sole authority to approve, modify, or disapprove research activities covered by these policies. The IO may veto any approval decisions made by the IRB but may not overrule disapprovals.

907. Required regulatory findings and determinations. The IRB is tasked to make certain regulatory findings for research under FDA jurisdiction (drugs, devices, and biologics), OHRP jurisdiction (federally funded), for certain vulnerable populations (prisoners, minors, pregnant women/fetuses). Regulatory determinations may be documented in the minutes, via checklists, or by letter or Board Action forms to the PI, or by any other method that adequately preserves and documents the required regulatory findings.

908. Voting, quorum, abstention. Federal regulations state 21CFR56.107(e) "No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB." IRB members must recuse themselves from participating in voting and deliberations of studies in which they have a

conflict of interest. This SOP provides guidance as to how to manage and document those circumstances in which an IRB member has a conflict of interest in studies under initial review as well as continuing review. In addition, this SOP defines the quorum requirements and provides clarification of what constitutes a majority in those cases when members recuse themselves or abstain.

- Abstention: When a member does not vote although they are present during the vote.
- Quorum: The minimum number of members necessary to conduct business; one more than half, including a member whose background is non-scientific.
- Recusal: When a member disqualifies themselves as part of the voting body.

909. Abstention by a member. An individual may abstain due to their inability to vote in favor of a study. They might also abstain because they have an association with the investigator or sponsor, but that association does not constitute a conflict of interest and requires their recusal. An individual who abstains from voting is still counted as part of the quorum. Abstention counts as a "no" vote, which may be a significant factor if there is a controverted issue.

910. IRB Member Conflicts of Interests. Conflicts of interest for IRB members arise when studies are reviewed in which a member is a principal investigator, key personnel, or paid consultant for a research study under review. A conflict of interest may also arise when an IRB member has financial relations with the sponsor outside of the conduct of the study under review. Professional association and administrative duties do not necessarily pose a conflict of interest if those relationships are known to the committee. For instance, pharmacy staff who are IRB members may review drug studies. Similarly, IRB members who are administrators may review studies that affect their departments, and IRB members who are physicians or nurses may be involved in reviewing studies conducted by their office partners if they are not named co-investigators or key personnel.

If members feel they have a potential conflict of interest, they should state this prior to their review and consider themselves out of quorum for that item. The IRB may decide whether the potential conflict should prohibit the member from voting or participating in the review.

An individual who recuses themselves due to a conflict of interest does not count towards the quorum. Although they may attend the meeting to answer questions, they must leave the room prior to deliberation and voting. The IRB must ensure that quorum is maintained when a member recuses themselves due to a conflict of interest.

911. Review of adverse events, unanticipated problems, protocol violations, subject complaints, or violations of governmental regulations or institutional policies. The IRB will assess serious adverse events, suspected or alleged protocol violations, subject complaints, or violations of governmental regulations or institutional policies. Such incidents or allegations may be referred to the IO for further investigation and action, as appropriate.

a. ADVERSE EVENT REPORTING

The Common Rule specifies that investigators "promptly report…all unanticipated problems involving risk to human subjects". Such reporting can vary greatly depending on the nature of the study. For treatment studies, an adverse event could be a treatment-related side effect or any of several physical injuries related or unrelated to the drug or device. For studies that don't involve treatment, an adverse event could be a breach of confidentiality. Some studies define the range of adverse events that must be reported while others refer to FDA definitions as to what constitutes an adverse event that must be reported to the IRB.

Adverse Event - Any untoward medical occurrence in a patient or clinical investigation subject administered an investigational product that does not necessarily have a casual relationship with this treatment. An adverse event can be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product. Adverse events are routinely reported to sponsors but not to the IRB.

Serious Adverse Event -Any experience that suggests a significant hazard, contraindication, side effect, or precaution and any experience that is fatal or life-threatening, is permanently disabling, requires in-patient hospitalization, or is a congenital anomaly, cancer, or overdose, whether it is related to an investigational drug or device therapy.

On-Site SAE - A Serious Adverse Event reported concerning a research subject enrolled in a clinical trial whose Principal Investigator is conducting that study either in their clinic in Portland or at an LH facility.

Off-Site SAE - A Serious Adverse Event reported concerning a research subject who was enrolled at a site outside the LH.

IND Safety Report - An off-site SAE report generated by the sponsor and forwarded to the principal investigator.

DSMB – A Data Safety and Monitoring Board is an organization responsible for analyzing adverse events in multi-site studies.

Investigators Brochure - A compilation of the clinical and nonclinical data on the investigational product that is relevant to the study of the investigational product in human subjects.

On-Site Reports: All on-site Serious Adverse Events must be reported to the LHS IRB within 10 working days. If a sponsor defines Serious Adverse Events in a different manner than specified below, then a copy of that definition must be submitted, and reporting will follow the sponsor's guidelines. In any case, all deaths of research subjects, whether on therapy or in follow-up, will be reported to the LH IRB within 10 working days after the investigator becomes aware that the research subject has died. All on-site Serious Adverse Events will be acknowledged by the IRB chair or vice-chair.

Off-site Reports: Off-site Serious Adverse Event reports may be handled in several ways. If the off-site SAE does not affect the protocol or consent form, they do not have to be sent to the Legacy IRB. If the sponsor requests that they be submitted, they may be reported to the IRB individually, in

groups of 10-20, monthly, quarterly, or annually. Investigators are strongly discouraged from sending all IND safety reports to the IRB unless they provide information related to the representation of risk in the consent form. The LH IRB prefers to receive IND safety reports accompanied by analysis from the sponsor's DSMB. Investigators and sponsors may negotiate with the Legacy IRB with the initial application or with an amendment regarding the submission and acknowledgment of off-site SAEs based on the nature of the study and the condition of the subjects.

912. Suspension or termination of research. The IRB has the authority to suspend or terminate approval of research that is not conducted in accordance with the IRB's requirements or that has been associated with serious harm to subjects. The IO, the Chair, or the Chair's designee may be authorized to take immediate action to suspend IRB approval of research for any serious noncompliance or unanticipated problems involving risks to subjects or others.

913. Documentation of suspension or Termination of research. Any suspension or termination of approval will include reasons for the IRB's actions and will be reported promptly to the investigator, the IO, and federal officials as required.

914. No override of IRB disapproval. No external body or official may override IRB disapprovals, nor apply undue pressure on the board to reverse a decision. The board may, upon the request of an investigator or on its own initiative, reconsider any proposal and reverse its own determination.

915. Continuing Review. The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. The IRB will request that the PI update the committee on the progress of the investigation to include whether all serious adverse events have been reported and whether the study is being conducted according to the approved protocol. The IRB may request a continuing review at any time interval and may request additional information regarding the study. Continuing approval by the IRB requires that the research continues to meet the criteria of approval under 45 CFR 56.111.

Although certain types of continuing review may be conducted under the expedited review procedure, (e.g., minimal risk studies, studies in which no subjects have been enrolled or research that is permanently closed to subject enrollment), continuing reviews is typically conducted by the full IRB. Any member may propose through motion that a minimal risk study be moved to continuing review via expedited review, and the IRB may vote on that motion.

Investigators are initially requested to submit a continuing review two months prior to the review date and given at least one reminder as the deadline approaches. Studies that do not comply with requests for review in a timely manner are suspended and instructed on how to reapply.

916. Duration of IRB Oversight. Continuing review by the IRB is required if investigators are either interacting or intervening with subjects for research purposes or accessing identifiable private information and PHI for research purposes. For multi-site research, it is acceptable to close the study if investigators are neither interacting with nor accessing subject information, as outlined above.

917. IRB review of PI non-compliance, deviations, violations, unanticipated problems, corrective actions, and board findings, determinations, and actions.

a. IRB Actions. The protocol approved by the IRB must be followed or amended. Adherence to the approved protocol is not always possible, and in some cases, incidences of non-compliance or deviation or violations must be reported to the IRB to help determine whether appropriate safeguards are in effect, whether there has been serious or continuing non-compliance, appropriate corrective actions taken, and whether the consent form provides adequate information for a subject to provide informed consent.

b. Protocol Deviation. A protocol deviation occurs when provisions of the protocol were not followed due to non-compliance by the research subject or by study staff

c. Protocol Violation. A protocol violation occurs when the investigator or other staff deviate from the provisions of the protocol. Examples include failure to obtain informed consent, enrollment of a subject who does not meet the inclusion/exclusion criteria, failure to perform a required lab test, medication dispensing error, failure to follow the safety monitoring plan, implementation of unapproved recruitment procedures, or over-enrollment of the approved number of subjects, failure to submit continuing review application prior to the IRB expiration date or conducting any study procedures not approved by the IRB.

d. Protocol Exception. A protocol exception occurs when provisions of the protocol were not followed due to a decision made by the investigator or by the sponsor. Examples include subject visits occurring outside of visit windows.

e. Deviations and Violations. Protocol deviations and violations are events not approved by the IRB. These activities need to be reported to the sponsor but should usually only be reported to the IRB if they involve endangering the safety of the research subject or violating the rights of the research subject. Reportable events should be submitted to the IRB within five working days. That report should be in the form of a letter documenting the mistake and providing a process or corrective action plan by which to prevent further similar mistakes. In some cases, violations and deviations may also result in a serious adverse report. Major deviations and violations should be summarized in the narrative report requested at the time of continuing review.

f. Exceptions. An exception may be granted in advance through a waiver by the sponsor or may be the result of a physician's decision that is in the best interest of the research subject. In those instances when adequate time exists, waivers must also be approved by the IRB. This should be done using the Modification Form. In those instances where there is not adequate time to consult the IRB, waivers must be reported within five working days. This report should be in the form of a letter documenting the waiver. If the investigator can anticipate that a similar situation may arise in the future, then they must submit a protocol amendment to be reviewed by the IRB. Exceptions that do not lead to protocol amendments should be summarized in the narrative report requested at continuing review.

g. Medical Monitor. Some treatment studies employ a medical monitor to provide safety oversight. In those cases, medical monitors may authorize PIs to deviate from the protocol to ensure patient safety. These decisions may be made with and without the approval of the IRB. In those instances where there is no time to request a variance from the protocol, the PI must report the activity to the IRB within five working days. In other instances, when time allows, the medical monitor may make recommendations regarding inclusion/exclusion criteria and other protocol-related details that should be submitted to the IRB for review and approval prior to instituting those changes.

918. Review of Emergency Use Requests.

The FDA regulates the development of drugs, devices and biologicals for the treatment of disease but does not regulate physician practice. The FDA allows physicians to treat patients with investigations agents outside of a clinical trial, and this policy is written to define those various circumstances, which include "emergency use", "emergency use IND", "compassionate use", "single patient IND", "treatment IND", "Group C Protocol" and "off label use of an HUD".

Although physician practice is managed by hospitals and state medical associations, the use of investigational agents, including drugs, biologicals, and devices, is also governed by FDA regulations. For the purposes of this policy, the following federal regulations are utilized to guide this policy: 21 CFR 50.23; 21 CFR 50.24; 21 CFR 56.102(d); 21 CFR 56.104(c); 21 CFR 56.105; 21 CFR 312.34; 21 CFR 312.35; 21 CFR 312.36

Due to the complexity of medical emergencies, the Legacy IRB policy provides a framework for physicians to understand their regulatory responsibilities to the institution, the manufacturer, and the FDA. Specifically, this policy seeks to address the physicians' need to seek prospective review and approval, notification, communication with the manufacturer and the FDA, and follow-up requirements.

The physician may not conclude that an "emergency" exists far enough in advance of the time when treatment may be needed. Institutional and FDA approval procedures may require more time than is available. Physicians should be aware that the FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the various procedures enough in advance to avoid creating a situation in which such arrangements are impracticable.

a. Emergency Use: An **emergency** is defined as a **life-threatening** or **severely debilitating** situation in a single patient for which there is no standard acceptable treatment and for which there is no time to obtain IRB approval [21 CFR 56.102(d)]. **Life-threatening** is defined [FDA Information Sheets] as diseases or conditions with a high likelihood of death unless the course of the disease is interrupted. **Severely Debilitating** is defined as diseases or conditions that cause major irreversible morbidity. Examples include blindness, loss of a limb, loss of hearing, paralysis, or stroke.

Emergency Use must meet **all** the following criteria:

1. a life-threatening/severely debilitating condition in which no standard acceptable treatment is available
2. an IRB approved protocol is not available
3. an investigational agent or device that might be beneficial, in the physician's opinion is available
4. a sponsor who can provide the agent and will work with the FDA is available
5. an emergency situation exists in which there is not sufficient time to obtain FDA or IRB approval to use

Emergency use meeting the above criteria is exempt from prior IRB review and approval, provided such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review [21CFR56.104(c)]. When emergency treatment is initiated without IRB review and approval, the patient data may not be included as research data or used in a report to the FDA. The FDA regulations do not provide for expedited approval in emergency situations. Some manufacturers will agree to allow the use of the drug, biologic, or device, but their policy requires "an IRB approval letter" before the test item will be shipped. If it is not possible to convene a quorum within the time available, the IRB chair or vice-chair may sign a letter acknowledging the emergency circumstances, but this should not be construed as IRB approval. Even for Emergency Use, informed consent should be sought. If the circumstances do not provide for the opportunity to obtain informed consent, the physician is required to submit the report within five days, accompanied by the determination of an independent physician that the treatment was appropriate, and that informed consent was impracticable.

In either case, whether the Emergency Use is being reported to the IRB or whether the physician is seeking a letter acknowledging the request for emergency use, the letter from the physician must contain the following information:

1. the patient's situation is life-threatening or severely debilitating
2. no standard treatment is available
3. there is no time to obtain prospective IRB approval
4. outline of the treatment plan
5. sponsor providing the investigational agent

Following the treatment, the physician is required to provide the IRB with a report of the patient's course and outcome.

a. **Emergency Use IND.** In some cases, the emergency use of an unapproved investigational device, drug, or biologic can be managed through an Emergency Use IND or IDE that is organized between the manufacturer and the FDA. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for emergency use under the company's IND/IDE.

In such cases, the FDA may authorize the shipment of the drug for a specified use [21 CFR 312.36]. Prospective IRB review is required unless the conditions for exemption are met [21 CFR 56.104(c) and 56.102(d)]. Informed consent is required unless the conditions for exception are met [21 CFR 50.23]. See the Emergency Use section above.

The Emergency Use IND/IDE differs from Emergency Use in that it involves a mechanism already created by the FDA and manufacturers who have anticipated that these situations may arise. The manner of requesting the Emergency Use IND/IDE is the same as outlined in the Emergency Use section of this policy and the reporting requirements are also the same. With an Emergency Use IND/IDE, sponsors may be allowed to collect safety data that is then shared with the FDA.

b. Single Patient IND/IDE or Treatment IND/IDE. The Single Patient IND/IDE, also called the Treatment IND/IDE [21 CFR 312.34 and 312.35] are mechanisms for providing eligible subjects with investigational drugs or devices for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND/IDE may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment IND/IDEs also serve to expand the body of knowledge about the drug or device. There are four requirements that must be met before a treatment IND/IDE can be issued:

1) the drug or device is intended to treat a serious or immediately life-threatening disease
2) there is no satisfactory alternative treatment available
3) the drug or device is already under investigation, or trials have been completed, and
4) the trial sponsor is actively pursuing marketing approval.

Treatment IND/IDE studies require prospective IRB review and informed consent. In most cases, the Treatment IND/IDE will be established outside of a single case but will be instituted for a class of patients where the need for such a treatment can be anticipated in advance.

For the Single Patient or Treatment IND/IDE, the following documents need to be submitted to the IRB for review:

1. Protocol
2. Investigator’s Brochure
3. Consent form
4. Physician’s biosketch and/or CV
5. Form 1572

The IRB may choose to review each case as it occurs or may simply request a follow up report on each case either as they occur or at specified intervals under Continuing Review.

c. Group C Protocol. The "Group C" treatment IND was established by agreement between the FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of

cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because the administration of Group C drugs is not done with research intent, the FDA has generally granted a waiver from the IRB review requirements [21 CFR 56.105]. Even though the FDA has granted a waiver for these drugs, an IRB may still choose to conduct a review under its policies and procedures. The usage of a Group C drug is described in its accompanying "Guideline Protocol" document. The Guideline Protocol contains an FDA-approved informed consent document which must be used if there has been no local IRB review. At Legacy, all Group C Protocols require prospective IRB review and approval.

d. Off Label and Emergency Use of a Humanitarian Use Device. Humanitarian Use Devices (HUD) are intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in fewer than 8000 individuals in the United States per year. The Legacy IRB is responsible for the initial as well as continuing review of the HUD. For the initial review of a HUD, IRBs are required to perform a full board review. For continuing review, however, IRBs may use the expedited review procedures (21 CFR 56.110) unless the IRB determines that full board review should be performed. The IRB is not required to review and approve individual uses of a HUD, although it may do so. The IRB may use its discretion to determine how to approve the use of the HUD. The IRB may approve the use of the HUD, for instance, without any further restrictions, under a protocol, or on a case-by-case basis. In reviewing the use of a HUD, IRBs should be cognizant that the FDA recommends that the use of the device not exceed the scope of the indication approved in the Humanitarian Device Exemption (HDE).

e. Emergency use of a HUD, on-label (without prior IRB approval of the HUD). If a physician in an emergency situation determines that IRB approval for the use of a HUD cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The physician must report the emergency use within five days and provide written notification of the use to the IRB chair, including identification of the patient involved, the date of use, and the reason for use.

f. Emergency use of a HUD, off-label (after prior IRB approval of the HUD). If the Legacy IRB has reviewed and approved a HUD and HDE, a physician faced with an emergency situation (i.e., not adequate time to obtain IDE from the FDA) may use a HUD outside its approved indication.

g. Use of a HUD after the LH IRB has approved the use of the HUD at LH facilities. If the LH IRB has reviewed and approved the use of a HUD, a physician may use the HUD for any indication (on- or off-label) without additional IRB review if s/he determines that there is no alternative device for the patient’s condition. The physician should obtain informed consent from the patient and ensure that reasonable patient

protection measures are followed, such as devising schedules to monitor the patient. Such off-label uses should be reported within 5 working days to the LH IRB.

DOMAIN 10: PRINCIPAL INVESTIGATOR ASSURANCES AND AGREEMENTS

1001. **PI assurances to the IRB.** The PI must make the following assurances to the Legacy IRB and agree by signing an application form upon submission of a research proposal.

- That the attestations that all the information in the research application is accurate.
- That when requesting approval of HIPAA full and partial waivers of authorization for protected health information, the PI is providing written assurance that:

    - the use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
    - an adequate plan to protect the identifiers from improper use and disclosure
    - an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, and
    - adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted
    - The research could not practicably be conducted without the waiver or alteration, and
    - The research could not practicably be conducted without access to and use of the protected health information.

- That protected health information will not be re-used or disclosed to any other person or entity except as permitted under this approval.
- The PI will read and abide by all of the Board requirements contained in the IRB Approval and other Legacy Health IRB correspondence, and if one or more of the Board's requirements are not acceptable to the PI, the PI may ask the Board to reconsider its requirements but may not enroll subjects until the issue is resolved by the Board.
- Only the Legacy IRB may approve the research to be conducted, and it may not begin until the Board grants final approval.
- The PI will promptly report to the Legacy IRB office any proposed changes in the activity, changes in the informed consent form, unanticipated problems involving risk to

subjects or others, including adverse reactions to biologicals, drugs, radioisotope labeled drugs, or medical devices, injury or harm.

- The PI will retain the documentary evidence of informed consent for at least three years after the proposed activity has been completed or discontinued.
- The Legacy IRB is obligated to continually review this activity and the PI agrees to furnish the Board relevant information for re-approval of this research as needed and that failure to provide the information may result in the expiration or termination of IRB approval.
- The PI agrees to accept responsibility for the project's ethical conduct and for protecting the rights and welfare of the subjects.
- The PI will personally conduct the research.
- That all study staff will have undergone training in human subject protection training prior to participating in the research and that documentation of staff training will be kept on file for inspection if requested.
- That IRB approval applies to research ethics and regulations only and that IRB approval does not obligate Legacy or any of its managers or Departments to proceed with the activation of the study.
- The PI will obtain Legacy manager permission from the head of the department in which the research will be conducted. The PI understands that failure to obtain such permission may result in IRB approval being suspended or terminated.
- As PI of a study, they are responsible for identifying and ensuring that resource impacts from this study on any Legacy Department are properly negotiated.
- A copy of the IRB approval and other study documents can be sent to the Legacy manager/supervisor of the site where the research will be conducted.
- All Legacy institutional policies will be followed during the conduct of this research.
- Conduct the research in accordance with the relevant current protocol approved by the IRB.
- The PI will protect the rights, safety, and welfare of subjects involved in the research.
- The PI will submit proposed modifications to the IRB prior to their implementation.
- The PI will not make modifications to the research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
- If research approval expires, stop all research activities, and immediately contact the IRB.
- The PI will retain research records as required by regulatory requirements.

1002. Non-compliance by PI. If the PI is alleged or found to be non-compliant with research requirements, the PI agrees that they must respond to IRB determinations in writing within 30 days of receipt of the IRB's findings by acknowledging receipt (if no corrective actions are required), agree to the corrective actions, propose additional actions, or appeal the IRB's determination. The response is to ensure that IRB will consider the response to decide whether additional information is needed regarding its determinations.

1003. Findings of Non-Compliance.
Noncompliance is any action or activity associated with the conduct or oversight of research involving human participants that fails to comply with either the research plan as approved by a designated IRB, or federal regulations or institutional policies governing human subject research.

Noncompliance may range from minor to serious, be unintentional or willful, and may occur once or several times.
Noncompliance includes failure to have protocols reviewed by the IRB as required and protocol deviations in protocols approved by the IRB, including deviations made in the interest of a single participant, such as changing a participant's scheduled study visits. Noncompliance may result from the action of the investigator, research personnel, or a participant, and may or may not impact the rights and welfare of research participants or others or the integrity of the study. Complaints or reports of noncompliance from someone other than the Principal Investigator or study team personnel are handled as allegations of noncompliance until such time that the report is validated or found to be invalidated or dismissed.

1004.Minor Noncompliance:
Any behavior, action, or omission in the conduct or oversight of research involving human participants that deviates from the approved research plan, federal regulations, or institutional policies but, because of its nature, the research project, or subject population, does or did not:

1. harm or pose an increased risk of substantive harm to a research participant
2. result in a detrimental change to a participant's clinical or emotional condition or status
3. have a substantive effect on the value of the data collected, and
4. result from willful or knowing misconduct on the part of the investigator(s) or study staff.

Examples of minor noncompliance may include, but are not limited to, the following:

- Changing study personnel without notifying the IRB
- Shortening the duration between planned study visits
- Implementing minor wording changes in study questionnaires without first obtaining IRB approval
- Routine lab missed at a scheduled visit and re-drawn later

1005.Serious Noncompliance:
Any behavior, action, or omission in the conduct or oversight of human research that, in the judgment of a convened IRB, has been determined to:

1. adversely affect the rights and welfare of participants
2. harm or pose an increased risk of substantive harm to a research participant
3. result in a detrimental change to a participant's clinical or emotional condition or status
4. compromise the integrity or validity of the research, or
5. result from willful or knowing misconduct on the part of the investigator(s) or study staff.

Examples of serious noncompliance may include, but are not limited to, the following:

- Conducting non-exempt research that requires direct interaction or interventions with human participants without first obtaining IRB approval

 Enrolling participants who fail to meet the inclusion or exclusion criteria in a protocol that involves greater than minimal risk and that, in the opinion of the IRB Chair, designee, or convened IRB, places the participant(s) at greater risk
 Failing to submit a continuing review application to the IRB before study expiration for an ongoing study
 Failing to obtain and/or document a participant's informed consent, provided the IRB has not granted a waiver of consent
 Failing to retain copies of signed informed consent forms
 Performing a study procedure not approved by the IRB; or failing to perform a required study visit or procedure that, in either case, may affect subject safety or data integrity
 Failing to follow the safety monitoring plan
 Enrolling study subjects after IRB approval of a study has expired, or
 Failing to report serious adverse events and/or unanticipated problems to the IRB in accordance with IRB Policy 710 Reporting Adverse Events and Unanticipated Problems.

1006. Continuing Noncompliance:
A pattern of noncompliance that, in the judgment of a convened IRB:

1. indicates a lack of understanding or disregard for the regulations or institutional requirements
that protect the rights and welfare of participants
2. compromises the scientific integrity of a study such that important conclusions can no longer be reached
3. suggests a likelihood that noncompliance will continue without intervention, or
4. involves frequent instances of minor non-compliance, for example, repetitive protocol deviations.

Examples of continuing noncompliance may include, but are not limited to, the following:

 Repeated failure to respond to requests from the IRB to resolve an episode of noncompliance or a pattern of minor noncompliance, such as repetitive protocol deviations, or
 Consistently late submissions of continuing review applications or other items that require prompt reporting to the IRB.

1007. IRB ACTIONS RELATED TO NON-COMPLIANCE.

The IRB may take the following actions related to non-compliance:

a. **Determination of non-compliance and requirement of corrective actions.** The IRB may find that corrective actions are needed and that a finding or determination of non-compliance will remain in place until corrective actions are taken. The specific corrective actions that are needed will be determined by the specific non-compliance findings.
b. **Suspension of study activity.** A suspension of temporary cessation of one or more aspects of an IRB-approved study while the research is considered active. The activities

to be suspended are determined by the specific concerns raised and the potential risks to participants of continuing or not continuing study procedures and must be either determined by or endorsed by the IRB. Suspensions may apply to some or all protocol activities, such as stopping further enrollment of new participants or stopping all protocol-related activities. (45 CFR §46.113 and 21 CFR §56.113)

c. **Termination.** Termination is the withdrawal of IRB approval of a study. Following a determination to terminate a study, no study procedures may occur other than those identified by the IRB as necessary for the orderly closing of the study. (45 CFR §46.113 and 21 CFR §56.113)

1008. Closure of the research. The PI agrees to submit a closure report when:

- The protocol is permanently closed to enrollment
- All subjects have completed all protocol-related interventions and interactions
- For research subject to federal oversight other than the FDA:
    - No additional identifiable private information about the subjects is being obtained
    - Your analysis of private identifiable information is completed

PART C: LEGACY HEALTH POLICIES FOR HUMAN SUBJECT RESEARCH

LEGACY HEALTH

ADMINISTRATIVE

Policy #: **100.18**
Origination Date: **12/93** **Board Approval: 9/22**
Last Revision Date: **09/22**

SECTION: **ADMINISTRATION & MANAGEMENT**
TITLE: **BIOMEDICAL AND CLINICAL RESEARCH - HUMAN SUBJECTS' PROTECTION, INSTITUTIONAL REVIEW BOARD AND USES AND DISCLOSURES OF PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES**

FACILITY:

☐ Legacy Emanuel Hospital and Health Center
(as applicable: ☐ LEMC only ☐ RCH only ☐ Unity Center for Behavioral Health only)

☐ Legacy Good Samaritan Medical Center	☐ Legacy Medical Group
☐ Legacy Meridian Park Medical Center	☐ Legacy Urgent Care
☐ Legacy Mount Hood Medical Center	☐ Legacy Lab Services
☐ Legacy Salmon Creek Medical Center	☐ Legacy Visiting Nurse Association (Hospice)
☐ Legacy Silverton Medical Center	☒ Legacy Research Institute
☐ Administrative/System Support Services	☐ Other:

CONTENTS

PURPOSE:

1. To assure the conduct of all research activities and reviews of studies involving human volunteers and patients within Legacy Health are uniform, and in compliance with all applicable policies, regardless of funding source or relationship of the research investigator to the institution.

2. To ensure protection of human subjects in biomedical and clinical research.

3. To assure that studies involving the use of human subjects are in full compliance with the policies and regulations of Legacy Health, the Department of Health and Human Services (DHHS), the Federal Food and Drug Administration (FDA), and Oregon State Law.

4. To assure that all research proposals which involve human subjects are without exception reviewed by the Legacy Institutional Review Board (IRB). Review includes full board review, expedited review, and exemption determinations.

5. To assure mechanisms for determining the circumstances for ceding IRB oversight of a study to an external IRB for single IRB (sIRB) or central IRB purposes.
6. To establish the conditions under which protected health information ("PHI") may be used or disclosed by Legacy Health for research purposes.

DEFINITIONS:

1. **Human Subject –** A living individual about whom an investigator conducting research obtains (I) data through intervention or interaction with the individual, or (2) individually identifiable information.
2. **Institutional Review Board (IRB) –** A board charged with protecting the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable Legacy policies as well as state and federal regulations.
3. **Interaction –** Communication or interpersonal contact between investigator and subject.
4. **Intervention –** Physical procedures by which data is gathered and manipulations of the subject or the subject's environment that are performed for research purposes.
5. **IRB Approval –** The determination of the IRB that the research has been reviewed and may be conducted at Legacy within the constraints set forth by the IRB and by other institutional and Federal requirements.
6. **Minimal Risk –** The probability and magnitude of harm or discomfort anticipated by 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.
7. **Protected Health Information –** Any information that 1) is received by a health care provider, health plan or clearinghouse, 2) is transmitted electronically or maintained in any other form or medium (including oral), 3) relates to the provision of or payment for health care for a patient or to the past, present or future physical or mental health condition of a patient, and 4) is individually identifiable. Information is presumed to be de-identified if all of the following identifiers have been removed or concealed:
    a. patient name;
    b. street address, zip code, city;
    c. phone number;
    d. fax number;
    e. email address;
    f. birth date, admission date, discharge date, date of death, all ages over 89;
    g. social security number;

h. medical record number;
i. account number;
j. health plan beneficiary number;
k. certificate/license number;
l. vehicle ID number, license plate number;
m. device identifier number and serial number;
n. Web Universal Resource Locator number;
o. Internet Protocol (IP) address;
p. fingerprints, voice prints, other biometric identifier;
q. full face photographic images; or
r. any other unique identifying number, characteristic or code and any associated health information.

8. Quality Improvement – A systematic investigation designed to develop knowledge to be used within the department or institution to improve services, procedures or treatment.
9. Research – A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
10. Single IRB (sIRB) Request – a request from a investigator, sponsor, or other stakeholder to cede IRB oversight to external IRB dues to federal funding requirements.

POLICY:

A. Responsibilities

1. Legacy Health, as a participant in research involving human subjects shall:
   a. Be guided by the ethical principles regarding all research involving humans as subjects as set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research entitled Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report").
   b. Adopt the broad tenets of the Declaration of Helsinki as institutional policy in protecting the rights and welfare of research subjects.
   c. Apply the appropriate federal regulations to research that is federally funded or sponsor by federal agencies as required by law and regulation.
   d. Apply the appropriate federal regulations to research that falls under the jurisdiction of the Food and Drug Administration (FDA).
   e. Encourage continuing constructive communication between the IRB and the research investigator as a means of safeguarding the rights, safety, and welfare of human subjects.
   f. Have available the necessary resources required for human subjects who may suffer physical, psychological, or other injury as a result of participation in research activities.
   g. Acknowledge that it will bear full responsibility for the proper performance of all work and services including the use of human subjects under federal grant or contract covered by the general assurance, including compliance with pertinent federal, state or local laws, particularly those concerned with informed consent including the use or disclosure of protected health information ("PHI") for research purposes.
   h. Maintain all documentation of informed consent, authorization and waiver of authorization as it pertains to research activities conducted within Legacy Health for a period not inconsistent with law or regulation.
   i. Have the right to disapprove the conduct of any research study, even where it has received IRB approval. However, consistent with federal regulations, Legacy Health may not approve a research study which a duly qualified IRB has not approved.

2. Legacy Research Institute (LRI) shall implement policies, rules, regulations and procedures for the proper safeguarding of the welfare of human subjects participating in all forms of research at Legacy Health sites, including Legacy partners and collaborations. .
   a. Maintain appropriate records of the IRB's review of scientific protocols, applications, activities, of documentation of informed consent, authorization and waiver of authorization, documentation that may pertain to the selection, participation and protection of subjects, and to the review of circumstances that adversely affect the rights or welfare of individual subjects.
   b. At least annually, reaffirm through appropriate administrative overview that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied and are consistent with the regulations and assurances as accepted by federal, state and local agencies.

3. LRI, as the research arm of Legacy Health, will establish and maintain an Institutional Review Board competent to review projects and activities that involve human subjects. The responsibilities of the IRB are detailed in Attachment #1 of this policy.

B. Legal Considerations

1. Members of the IRB are responsible for familiarizing themselves with the ethical requirements, statutes, regulations and common law precedents which may govern their duties and responsibilities through consultation with regulatory specialists and/or legal counsel.

2. The provisions of this policy may not be construed in any manner or sense that would abrogate, supersede or moderate more restrictive applicable law or precedential legal decision.

C. Informed Consent

No research involving human subjects may be conducted unless (1) an informed consent to participate in the research study is obtained from the research subject; or (2) a waiver of informed consent has been approved by the IRB.

D. Privacy Rule

1. General Rule. No research involving uses or disclosures of a subject's PHI may be conducted unless (a) an authorization for use or disclosure of such information is obtained from the subject, (b) a waiver of authorization has been approved by an IRB) (or a Privacy Board, as applicable), (c) the health information has been de-identified, (d) the health information is used or disclosed in a limited data set in accordance with a data use agreement, or (e) one of the exceptions listed in Part 2 below applies.

2. Exceptions. The following circumstances shall be exceptions to the Privacy Rule requirements of this policy:
   a. A subject's PHI may be disclosed to a person subject to the jurisdiction of the Food and Drug Administration (FDA) with respect to an FDA-regulated product or activity for which that person has responsibility, for the purpose of activities related to the quality, safety or effectiveness of such FDA-regulated product or activity, including but not limited to: (i) collecting or reporting adverse events, product defects or problems, or biological product deviations, (ii) to track FDA-regulated products, (iii) to enable product recalls,

repairs, replacement or look back activities, or (iv) to conduct post marketing surveillance.

b. Protected health information may be used by or disclosed to a researcher as necessary to prepare a research protocol or for similar purposes preparatory to research provided the researcher represents to Legacy Health that: (i) the use or disclosure is sought solely for such purposes, (ii) no protected health information will be removed from Legacy Health's premises by the researcher in the course of the review, and (iii) the protected health information for which use or access is sought is necessary for the research purposes.

c. Protected health information may be used by or disclosed to a researcher for research on decedents provided the researcher: (i) represents to Legacy Health that the use or disclosure is sought solely for research on the protected health information of decedents, (ii) provides to Legacy Health, upon request, documentation of the death of the research subject, and (iii) represents to Legacy Health that the protected health information is necessary for the research.

PROCEDURES:

1. Informed Consent. Informed Consent is the process by which information is presented to an individual to enable such individual to voluntarily decide whether or not to participate as a research subject. An informed consent is documented by the use of a written consent form approved by the IRB and signed by the subject. Such consent form will be provided to a subject in the following manner prior to such subject's participation unless a waiver of informed consent is approved by an IRB:

    Written. A written consent document that embodies all of the elements set forth in Part 1.a below is signed by the subject, a copy of which is given to the subject. Informed consent presented orally to the subject or the subject's legal representative shall be effective for medical research studies at Legacy Health only if the oral consent is consistent with law or regulation and has been approved by the IRB.

    a. Informed Consent Criteria. The informed consent shall be written in understandable language and contain the following criteria:
        (1) a statement that the study involves research, an explanation of the purposes of the research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of experimental procedures;
        (2) a description of reasonably foreseeable risks and discomforts to the subject;
        (3) a description of any benefits to the subject or to others which may be reasonably expected from the research;
        (4) a disclosure of appropriate alternative treatments that might be advantageous;
        (5) a statement describing the extent to which the confidentiality of records will be maintained;
        (6) an explanation of whether compensation will be paid and if injury occurs, whether treatment is available and where further information may be obtained;
        (7) an explanation of whom to contact about the research, the subject's rights and any research related injury; and
        (8) a statement that participation in the research study is voluntary, and refusal to participate or discontinuance with the study carries no penalty or loss of benefits to which the subject is otherwise entitled.

b. Additional Criteria. The informed consent should also provide one or more of the following provisions when applicable:
   (1) a statement that the treatment or procedure may involve currently unforeseeable risks to the subject (or to the embryo or fetus for subjects who are or may become pregnant);
   (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 study;
   (4) the consequences of a subject's decision to withdraw from the research and procedures of how a subject may terminate his or her participation;
   (5) a statement that significant new findings developed during the course of 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.
c. Exculpatory Language. The informed consent shall not contain any exculpatory language or release of Legacy Health, an investigator, sponsor or other institution.
d. Form. Authorization: In addition to informed consent under Part 1.a above, for uses and disclosures of protected health information for research purposes under the Privacy Rule, an authorization must be obtained from the research subject unless a waiver of authorization is approved by an IRB or Privacy Board, the information is de-identified, the protected health information is disclosed in a limited data set pursuant to a data use agreement, or one of the authorization exceptions set forth above applies.
e. When requesting an authorization from a subject, Legacy Health shall use an authorization form that contains:
   (1) a description of the information to be used or disclosed;
   (2) identification of the persons or class of persons authorized to make the use or disclosure;
   (3) the identification of the persons or class of persons to whom the information may be disclosed;
   (4) an expiration date or expiration event that relates to the individual or the purpose of the disclosure, which expiration date or event may be "none", "end of research study" or similar language;
   (5) a description of each purpose of the requested use or disclosure;
   (6) a statement of the right to revoke the authorization in writing, procedures to revoke the authorization and exceptions to the right to revoke,
   (7) a statement that information used or disclosed pursuant to an authorization may be subject to redisclosure and may no longer be protected by the federal privacy protections;
   (8) the signature of the subject and date; or if the authorization is signed by a personal representative of the subject, a description of such representative's authority to act for the subject;
   (9) a statement regarding the ability or inability of Legacy Health to condition treatment, payment, enrollment or eligibility for benefits on the authorization by stating either: (i) Legacy Health may not condition treatment, payment, enrollment or eligibility for benefits on whether the participant signs the authorization when such prohibition applies, or (ii) if Legacy Health is permitted to place such conditions, then an explanation of the consequences of the participant's refusal to sign the authorization.
f. The authorization may be in the same document as the Common Rule informed consent to participate in research, and as any optional consent to use or disclose protected health information for treatment, payment or health care operations. Legacy Health's

Compound Consent and Authorization Form can be found on Legacy's Public Folders, System Wide – Research.

g. The authorization must be written in plain language.
h. Legacy Health will provide the individual with a copy of the signed authorization.

2. Waiver of informed consent and/or authorization: When relying on a waiver or alteration of the (i) informed consent to participate in a research study and/or (ii) authorization requirements to use or disclose PHI for research purposes, the IRB (or Privacy Board, as applicable) shall document the following:
   a. Waiver of Informed Consent. An IRB can approve a waiver of informed consent if:
      (1) The research is to be conducted by or subject to the approval of state or local government officials, and is designed to study (i) a public benefit or service program, (ii) procedures for obtaining benefits or services under those programs, (iii) changes or alternative to those programs or procedures, and (iv) changes to payment methodology; or
      (2) For other research purposes, (i) the research involves no more than minimal risk to the subjects, (ii) the waiver or alteration does not adversely affect the rights and welfare of the subjects, and (iii) whenever appropriate, the subjects are provided with additional pertinent information after the conclusion of their participation in the study.
   b. Waiver or Alteration of Authorization. An IRB or Privacy Board can approve a waiver or alteration of authorization if:
      (1) Identification of the IRB (or Privacy Board) approving the waiver or alteration and the date of the approval, documentation of the waiver or alteration, and documentation of what PHI was disclosed pursuant to the waiver or alteration, to whom the disclosure was made and the date(s) of such disclosure(s).
   c. Criteria for Waiver/Alteration of Authorization.
      (1) The IRB or Privacy Board shall approve the waiver or alteration of the authorization requirement only if it can document that the following criteria for the waiver or alteration have been met:
         (i) The use or disclosure of protected health information involves no more than minimal risk to the individuals or their privacy, based on (A) an adequate plan to protect identifiers from improper use and disclosure, (B) an adequate plan to destroy the identifiers at the earliest opportunity (unless there is a health or research justification for retaining identifiers or such retention is otherwise required by law), and (C) adequate assurances that the protected health information will not be reused or disclosed to any other person or entity except as required by law, for authorized oversight of the research project, or for other research permitted under this policy.
         (ii) The research could not practicably be conducted without the alteration or waiver, and
         (iii) The research could not practicably be conducted without access to and use of the protected health information.
      (2) The IRB or Privacy Board shall approve the waiver or authorization only if, in addition to the documentation required by Part 3.b above, the IRB or Privacy Board includes in the waiver or alteration approval document the following:
         (i) a brief description of the protected health information to be used or disclosed;
         (ii) a statement that the alteration or waiver of authorization has been reviewed and approved by the IRB (or Privacy Board) under normal or expedited procedures; and
         (iii) the signature of the Chair or other member, as designated by the Chair, of the IRB (or Privacy Board).

3. De-identification: Legacy Health is not required to satisfy the authorization requirement if an IRB or Privacy Board determines that the health information is de-identified. Health information is de-identified only if:
   a. a person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable determines that the risk is very small that the information could be used alone or in combination with other reasonable available information by an anticipated recipient to identify a subject and documents the methods and results of the analysis that justify the determination, or
   b. the following identifiers of the subject or relatives, employers, or household members of the subject are removed, and Legacy Health does not have any actual knowledge that the information could be used alone or in combination with other information to identify the subject:
      (1) Names,
      (2) Geographic subdivisions smaller than a state (except the initial three digits of a zip code if the division contains more than 20,000 people),
      (3) All elements of dates except year (and for ages greater than 89, age unless grouped together into a single category of age 90 or older),
      (4) Telephone numbers,
      (5) Facsimile numbers,
      (6) Electronic mail addresses,
      (7) Social security numbers,
      (8) Medical record numbers,
      (9) Health plan beneficiary numbers,
      (10) Account numbers,
      (11) Certificate/license numbers,
      (12) Vehicle identification numbers,
      (13) Device identifiers,
      (14) Web universal resource locators,
      (15) Internet protocol addresses,
      (16) Biometric identifiers (e.g., finger/voice prints),
      (17) Full face photographic and any comparable images,
      (18) Any other unique identifying number characteristic or code, provided, however, that a code used by Legacy Health to re-identify the de-identified information is permitted so long as the code is not derived from or related to information about the subject and Legacy Health does not use or disclose the code for any other purpose and does not disclose the mechanism for re-identification.

4. Limited Data Set: Legacy Health may use protected health information to create a limited data set, or disclose protected health information to a business associate to create a limited data set, for research purposes so long as Legacy Health obtains satisfactory assurance, in the form of a data use agreement, that the limited data set recipient will only use the protected health information for limited purposes.
   a. A limited data set is protected health information that excludes the following direct identifiers of the subject or of relatives, employers, or household members of the subject:
      (1) Names,
      (2) Postal address information,
      (3) Telephone numbers,
      (4) Fax numbers,
      (5) Electronic mail addresses,

(6) Social security numbers,
(7) Medical record numbers,
(8) Health plan beneficiary numbers,
(9) Account numbers,
(10) Certificate/license numbers,
(11) Vehicle identification numbers and serial numbers (including license plate numbers),
(12) Device identifiers and serial numbers,
(13) Web Universal Resource Locators,
(14) Internet Protocol address numbers,
(15) Biometric identifiers (including finger and voice prints), and
(16) Full face photographic images and any comparable images.

b. A data use agreement between Legacy Health and the limited data set recipient must:
   (1) establish that the recipient will only use and disclose the limited data set information for purposes of research, public health or health care operations,
   (2) establish who is permitted to use or receive the limited data set,
   (3) provide that the recipient will:
      (i) not use or further disclose the limited data set information other than as permitted by the data use agreement or as otherwise required by law,
      (ii) use appropriate safeguards to prevent use or disclosure of the limited data set information other than as provided for by the data use agreement,
      (iii) report to Legacy Health any use or disclosure of the limited data set information other than as provided for in the data use agreement,
      (iv) ensure that any agents, including a subcontractor, to whom the recipient provides the limited data set information agrees to the same restrictions and conditions that apply to the recipient, and
      (v) not identify the limited data set information or contact the subjects.
c. Legacy Health's sample Data Use Agreement can be found on Legacy's Public Folders, System Wide – Research.

References: Common Rule, 45 CFR § 46.101 et seq.
HIPAA Privacy Regulations, 45 CFR §§160-164
Legacy Standards 700.15, 700.17

Approved by: Legacy Research
Legal
Operations Team
MQ&C
Legacy Health Governing Board of Directors

Originator: Legacy Research

ATTACHMENT 1

THE INSTITUTIONAL REVIEW BOARD (IRB)

1. LRI will establish and maintain an Institutional Review Board competent to review projects and activities that involve human subjects. The IRB Chairperson and membership will be appointed by the Vice President of Research. The term of appointment will be at least two years and may be renewed if deemed necessary or desirableThe Vice President of Research may veto any approval granted by the IRB. However, , the VP of Research may not approve of an activity that has been disapproved by the IRB.

2. Responsibilities of the Chairperson include, but are not limited to, conducting the meeting of the IRB, assist in expedited review of protocols, changes in research and informed consent and authorization forms, review of requests to use investigational drugs in emergency/life threatening situations, and advising the VP of Research on whether a study may or should be overseen by an external IRB under a sIRB request.
3. The members of the IRB shall be selected to allow competent assessment of applications and proposals with regard to: the safety and protection of human subjects, compliance with national, local, and institutional policies and regulations, any applicable laws, standards of professional conduct and practice, Legacy Health policies, and community standards. The IRB must be sufficiently qualified through the maturity, experience, and expertise of its members. The IRB must also show sufficient diversity in its members' racial and cultural backgrounds. The IRB shall not consist entirely of members of a single professional group, nor entirely of men or of women. The IRB shall include at least one member whose primary concerns are in non-scientific areas. In addition, the IRB shall not consist entirely of persons who are officers, employees, or agents of Legacy Health but shall include at least one member who is not otherwise affiliated with Legacy Health, and who is not part of the immediate family of a person affiliated with Legacy Health. The membership of the IRB shall consist of the minimum of members required by federal regulations with quorum constituting a majority of the membership present, and of which at least one must be a non-scientific member.

4. The IRB has the responsibility to review, and the authority to approve, disapprove or require changes to all research activities involving human subjects. The IRB shall have authority to suspend or terminate approval of a research activity that is not being conducted in accordance with the IRB's decisions, conditions and requirements or that has been associated with unexpected serious harm to subjects of others, or investigator non-compliance.

5. The IRB shall approve research activities involving human subjects based on the IRB's determinations that the following requirements are satisfied:

    a. Risks to subjects are minimized:
        1) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
        2) Whenever appropriate by using procedures already being performed on the subjects for diagnostic or treatment purposes.
    b. Risks are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would

receive even if not participating in the research). The IRB shall not consider the anticipated long-range effects of applying knowledge gained in the research as among those research risks that fall within the purview of its responsibility.

c. Selection of subjects is equitable. In making this assessment the IRB shall take into account the purposes of the research, the setting in which the research will be conducted, and the population from which subjects will be recruited.
d. Informed consent will be obtained from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 21 CFR 50.20.
e. Informed consent will be appropriately documented, in accordance with, and to the extent required by 21 CFR 50.27.
f. Authorization/waiver of authorization will be obtained and appropriately documented, in accordance with and to the extent required by 45 CFR 164.508, .512, .514.
g. Advertising used to recruit human subjects is non-coercive and reflects truth in advertising.
h. Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
i. Make adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
j. The circumstances set forth above under Policy, Privacy Rule, Part 2 shall be exceptions from the requirements of this policy.

6. The IRB shall require documentation of informed consent by use of a written consent form, or may waive the requirement for the research investigator to obtain a signed consent form for some or all subjects if the IRB determines that:

   a. The research is to be conducted by or subject to the approval of state or local government officials, and is designed to study (i) a public benefit or service program, (ii) procedures for obtaining benefits or services under those programs, (iii) changes or alternative to those programs or procedures, and (iv) changes to payment methodology; or
   b. For other research purposes, (i) the research involves no more than minimal risk to the subjects, (ii) the waiver or alteration does not adversely affect the rights and welfare of the subjects, and (iii) whenever appropriate, the subjects are provided with additional pertinent information after the conclusion of their participation in the study.

   When the documentation requirement is waived, the IRB may require the research investigator to provide subjects with a written statement regarding the research.

7. The IRB shall have the authority to observe or have a third party observe the consent/authorization process and the research.

8. The IRB shall determine which projects need verification from sources other than the research investigators that no material changes have occurred since previous IRB review.

9. IRB reviews shall be conducted with objectivity and in a manner to ensure the exercise of independent judgment of the members. Members will be excluded from the total review process affecting projects or activities in which they have an active role or conflict of interest.

10. The review of certain studies may be eligible for an expedited review. See Attachment #2 for criteria and procedures.

11. The IRB shall utilize the following guidelines in conducting its review of studies which involve human subjects.

    a. All studies will be reviewed to assure that the rights and welfare of human subjects will be adequately protected.
    b. Studies will be reviewed to determine that the protocol meets the requirements of sound research design and is adequate and relevant to the established goals and objectives of the study.
    c. Informed consent and authorization will be obtained by use of an appropriately designed and completed consent form, or the conditions under which this process can be altered/waived will be defined and the documentation required will be delineated.
    d. A majority of the IRB must approve the proposal. A rejected proposal or consent/authorization form will be returned to the Principal Investigator for correction or revision.

12. The IRB office will at least annually reassure itself through internal review that its practices and procedures are being effectively applied and are consistent with federal, state and local regulations.

13. In cases of collaborative activities with other institutions where Legacy Health (LH) is the grantee or prime contractor, and LH obtains access to all or some of the subjects involved through one or more collaborating institutions, LH remains responsible for safeguarding the rights and welfare of the subjects. LH is therefore responsible for initial and continuing review of these activities. In such cases the IRB of LH shall request a concurrent review by the cooperating institutions of those portions of the protocol or activity which will involve human subjects for which the other institution has responsibilities.

14. In cases of collaborative activities with other institutions where LH is not the prime contractor, the IRB shall respond to the directions of the prime contractor without sacrificing its responsibilities for safeguarding the rights and welfare of human subjects involved at LH.

15. When the IRB accepts responsibility for review of research which is conducted by any independent investigator, Legacy Research will obtain and retain a Institutional Investigator Agreement (IIA) to document the investigator's commitment to abide: (1) by the same requirements for the protection of human research subjects as does LH and (2) the determinations of the IRB.

ATTACHMENT 2

CRITERIA AND PROCEDURE FOR EXPEDITED REVIEW

The eligibility of some research for review through the expedited procedure is in no way intended to negate or modify the policies of Legacy Health or the other requirements of 21 CFR 56.110.

The IRB may use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized.

The only research for which the IRB may use an expedited review procedure is that which involves no more than minimal risk to the subjects and in which the only involvement of human subjects will be in one or more of the following categories:

1. Collection of: hair and nail clippings, in a non-disfiguring manner, deciduous teeth; and permanent teeth if patient care indicates a need for extraction.

2. Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labor.

3. Recording of data from subjects 18 years of age or older using non-invasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (for example, x-rays, microwaves).

4. Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an eight-week period and no more often than two times per week, from subjects 18 years of age or older and who are in good health and not pregnant.

5. Collection of both supra- and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

6. Voice recordings made for research purposes such as investigations of speech defects.

7. Moderate exercise by healthy volunteers.

8. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

9. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the research investigator does not manipulate subjects' behavior and the research will not involve stress to subjects.

10. Research on drugs or devices for which an investigational new drug exemption or an investigational device exemption is not required.

11. Any other category specifically added to this list by the Department of Health and Human Services (DHHS) and published in the Federal Register.

Expedited review may be conducted by an IRB member designated by the VP of Research, IRB chair, or IRB Administrator/Senior Regulatory Specialist

The IRB member(s) conducting the expedited review may exercise all of the authorities of the IRB except that the reviewer(s) may not disapprove the research. The reviewer(s) shall refer any protocol which the reviewer(s) recommends be disapproved to the full committee for review. The reviewer(s) may also refer other protocols to the full committee whenever the reviewer(s) believes that full committee review for any reason is warranted.

When the expedited review procedure is used to approve a new research proposal, the IRB chairperson or member(s) conducting the review shall inform IRB members of the research protocols which have been approved under the procedure in a timely manner

At a convened IRB meeting, any member may request that an activity which has been approved under the expedited procedure be reviewed by the IRB in accordance with non-expedited procedures. A vote of the members shall be taken concerning the request and the majority shall decide the issue.

In cases where research activities were initially approved under expedited procedures and subsequently reviewed by non-expedited procedures, the decisions reached at the convened meeting shall supersede any decisions made through the expedited review.

ATTACHMENT 3

EMERGENCY, SINGLE PATIENT AND OTHER TREATMENT USES OF INVESTIGATIONAL AGENTS

BACKGROUND: The FDA regulates the development of drugs, devices and biologicals for the treatment of disease but does not regulate physician practice. The FDA allows for physicians to treat patients with investigations agents outside of a clinical trial and this policy is written to define those various circumstances which include "emergency use", "emergency use IND", "compassionate use", "single patient IND", "treatment IND", "Group C Protocol" and "off label use of an HUD".

AUTHORITY: Although physician practice is managed by hospitals and state medical associations, the use of investigational agents, including drugs, biologicals and devices is also governed by FDA regulations. For the purposes of this policy the following federal regulations are utilized to guide this policy: 21 CFR 50.23; 21 CFR 50.24; 21 CFR 56.102(d); 21 CFR 56.104(c); 21 CFR 56.105; 21 CFR 312.34; 21 CFR 312.35; 21 CFR 312.36

PURPOSE: Due to the complexity of medical emergencies, the Legacy IRB policy provides a framework for physicians to understand their regulatory responsibilities to the institution, the manufacturer and the FDA. Specifically, this policy seeks to address the physicians' need to seek prospective review and approval, notification, communication with the manufacturer and the FDA and follow up requirements.

The physician may not conclude that an "emergency" exists far enough in advance of the time when treatment may be needed. Institutional and FDA approval procedures may require more time than is available. Physicians should be aware that the FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the various procedures enough in advance to avoid creating a situation in which such arrangements are impracticable.

EMERGENCY USE: An **emergency** is defined as a **life-threatening** or **severely debilitating** situation in a single patient for which is no standard acceptable treatment and for which there is no time to obtain IRB approval [21 CFR 56.102(d)]. **Life-Threatening** is defined [FDA Information Sheets] as diseases or conditions with a high likelihood of death unless the course of the disease is interrupted. **Severely Debilitating** is defined as diseases or conditions that cause major irreversible morbidity. Examples include blindness, loss of a limb, loss of hearing, paralysis or stroke.

Emergency Use must meet **all** of the following criteria:

1. a life-threatening/severely debilitating condition in which no standard acceptable treatment is available
2. an IRB approved protocol is not available
3. an investigational agent or device that might be beneficial, in the physician's opinion in available
4. a sponsor who can provide the agent and will work with the FDA is available
5. an emergency situation exists in which there is not sufficient time to obtain FDA or IRB approval to use

Emergency use meeting the above criteria is exempt from prior IRB review and approval provided such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review [21CFR56.104(c)]. When emergency treatment is initiated without IRB review and approval the patient data may not be included as research data or used in a report to the FDA. The FDA regulations do not provide for expedited approval in emergency situations. Some manufacturers will agree to allow the use of the drug, biologic or device but their policy requires "an IRB approval letter" before the test item will be shipped. If it is not possible to convene a quorum within the time available, the IRB chair or vice-chair may sign a letter acknowledging the emergency circumstances, but this should not be construed as IRB approval. Even for Emergency Use informed consent should be sought. If the circumstances do not provide for the opportunity to obtain informed consent, the physician is required to submit the report within five days accompanied by the determination of an independent physician that the treatment was appropriate, and that informed consent was impracticable.

In either case, whether the Emergency Use is being reported to the IRB or whether the physician is seeking a letter acknowledging the request for emergency use, the letter from the physician must contain the following information:

1. the patient's situation is life-threatening or severely debilitating
2. no standard treatment is available
3. there is no time to obtain prospective IRB approval
4. outline of the treatment plan
5. sponsor providing the investigational agent

Following the treatment, the physician is required to provide the IRB with a report of the patient's course and final outcome.

EMERGENCY USE IDE/IND: In some cases, the emergency use of an unapproved investigational device, drug or biologic can be managed through an Emergency Use IND or IDE that is organized between the manufacturer and the FDA. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND/IDE.

In such cases, FDA may authorize shipment of the drug for a specified use [21 CFR 312.36]. Prospective IRB review is required unless the conditions for exemption are met [21 CFR 56.104(c) and 56.102(d)]. Informed consent is required unless the conditions for exception are met [21 CFR 50.23]. See Emergency use section above.

The Emergency Use IND/IDE differs from Emergency Use in that it involves a mechanism already created by the FDA and manufacturer who have anticipated that these situations may arise. The manner of requesting the Emergency Use IND/IDE are the same as outlined in the Emergency Use section of this policy and the reporting requirements are also the same. With an Emergency Use IND/IDE sponsors may be allowed to collect safety data that is then shared with the FDA.

SINGLE PATIENT IND/IDE OR TREATMENT IND/IDE: The Single Patient IND/IDE, also called the Treatment IND/IDE [21 CFR 312.34 and 312.35] are mechanisms for providing eligible subjects with investigational drugs or devices for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment

IND/IDE may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment IND/IDEs also serve to expand the body of knowledge about the drug or device. There are four requirements that must be met before a treatment IND/IDE can be issued:

1) the drug or device is intended to treat a serious or immediately life-threatening disease;
2) there is no satisfactory alternative treatment available;
3) the drug or device is already under investigation, or trials have been completed; and
4) the trial sponsor is actively pursuing marketing approval.

Treatment IND/IDE studies require prospective IRB review and informed consent. In most cases, the Treatment IND/IDE will be established outside of a single case but will be instituted for a class of patients where the need for such a treatment can be anticipated in advance.

For the Single Patient or Treatment IND/IDE the following documents need to be submitted to the IRB for review:

1. Protocol
2. Investigator's Brochure
3. Consent form
4. Physician's biosketch
5. Form 1572

The IRB may chose to review each case as it occurs or may simply request a follow up report on each case either as they occur or at specified intervals under Continuing Review.

GROUP C PROTOCOL: The "Group C" treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because administration of Group C drugs is not done with research intent, FDA has generally granted a waiver from the IRB review requirements [21 CFR 56.105]. Even though FDA has granted a waiver for these drugs, an IRB may still choose to conduct a review under its policies and procedures. The usage of a Group C drug is described in its accompanying "Guideline Protocol" document. The Guideline Protocol contains an FDA-approved informed consent document which must be used if there has been no local IRB review. At Legacy all Group C Protocols require prospective IRB review and approval.

OFF LABEL and EMERGENCY USE OF AN HUMANITARIAN USE DEVICE: Humanitarian Use Devices (HUD) are intended to benefit patients in the treatment and diagnosis of disease or condition that affect or are manifested in fewer than 4,000 individual in the United States per year. The Legacy IRB is responsible for initial as well as continuing review of the HUD. For initial review of a HUD, IRBs are required to perform a full board review. For continuing review, however, IRBs may use the expedited review procedures (21 CFR 56.110) unless the IRB

determines that full board review should be performed. The IRB is not required to review and approve individual uses of a HUD, although it may do so. The IRB may use its discretion to determine how to approve use of the HUD. The IRB may approve use of the HUD, for instance, without any further restrictions, under a protocol, or on a case-by-case basis. In reviewing the use of a HUD, IRBs should be cognizant that the FDA recommends that the use of the device not exceed the scope of the indication approved in the Humanitarian Device Exemption (HDE).

Emergency use of a HUD, on-label (without prior IRB approval of the HUD)
If a physician in an emergency situation determines that IRB approval for the use of a HUD cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The physician must report the emergency use within five days; provide written notification of the use to the IRB chair, including identification of the patient involved, the date of use, and the reason of use.

Emergency use of a HUD, off-label (after prior IRB approval of the HUD)
If the Legacy IRB has reviewed and approved a HUD and HDE, a physician faced with an emergency situation (i.e., not adequate time to obtain IDE from FDA) may use a HUD outside its approved indication.

Use of a HUD after the LH IRB has approved the use of the HUD at LH facilities
If the LH IRB has reviewed and approved the use of a HUD, a physician may use the HUD for any indication (on- or off-label) without additional IRB review if s/he determines that there is no alternative device for the patient's condition. The physician should obtain informed consent from the patient and ensure that reasonable patient protection measures are followed, such as devising schedules to monitor the patient. Such off-label uses should be reported within 5 working days to the LH IRB.

LEGACY HEALTH

ADMINISTRATIVE

Policy #: 100.15
Origination Date: 12/93 **Board Approved: July 2022**
Last Review Date: 07/22

SECTION: ADMINISTRATIVE & MANAGEMENT
TITLE: OVERSIGHT AND COORDINATION OF CLINICAL BIOMEDICAL RESEARCH BY LEGACY RESEARCH INSTITUTE (LRI)

FACILITY:

☐ Legacy Emanuel Hospital and Health Center
(as applicable: ☐ LEMC only ☐ RCH only ☐ Unity Center for Behavioral Health only)

☐ Legacy Good Samaritan Medical Center	☐ Legacy Medical Group
☐ Legacy Meridian Park Medical Center	☐ Legacy Urgent Care
☐ Legacy Mount Hood Medical Center	☐ Legacy Lab Services
☐ Legacy Salmon Creek Medical Center	☐ Legacy Visiting Nurse Association (Hospice)
☐ Legacy Silverton Medical Center	☒ Legacy Research Institute
☐ Administrative/System Support Services	☐ Other:

PURPOSE:
To establish the guidelines for LRI's oversight of all biomedical research involving Legacy Health (LH) patients, facilities, sites, investigators, or resources: the intent being to facilitate pursuit of the highest quality research at LH. The scope of this policy includes all research that constitutes human subject research and that requires a signature of approval from the Institutional Official to facilitate grants and contracts. The goal of the policy is to ensure that proposed clinical biomedical research at Legacy Health is properly vetted by Legacy administrators, reviewed and approved by Legacy IRB, and overseen by competent and skilled Legacy researchers.

RESPONSIBLE STAFF:
The level of staff accountable for this policy includes all physicians, nurses, administrators and other health professionals involved in biomedical research at Legacy as well as all physicians who have a contract for services with Legacy or funding through the Legacy Foundations. As Institutional Official, the Vice President of Research will determine whether Legacy Research Institute will manage and facilitate any research grants awarded to responsible staff.

DEFINITIONS:
- **Clinical Trials –** Studies of drugs, devices or procedures involving Legacy patients. These studies may be of drugs and devices regulated by the Food & Drug Administration (FDA), or may be initiated by the Principal Investigator, a professional society, or through a grant from agencies such as the National Institutes of Health.
- **Institutional Review Board (IRB) –** A board charged with protecting the rights and welfare of human research subjects recruited to participate in research activities and to ensure compliance with applicable Legacy policies as well as state and federal regulations (see LH100.18).

- **Principal Investigator (PI) –** An individual who submits a clinical trial to the IRB and upon IRB approval obtains authority to personally supervise, conduct and complete the study.
- **Research –** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge through publication, presentation or providing evidence for submission to the FDA.
- **Quality Improvement –** An investigation not primarily designed to develop or contribute to generalizable knowledge but to be used within the department or institution in which it was created to improve processes and services.

POLICY:
Legacy Health assigns Legacy Research Institute (LRI) responsibility for reviewing, overseeing, and superintending all medical research, clinical investigations, and all clinical studies for the testing and evaluation of pharmaceuticals, drugs and medical devices, novel therapies or practices, within LH. Under this policy, LRI will determine whether administration, vetting, review and overseeing a clinical study may be ceded to another department or institution. As such, LRI is tasked with:

1. Centralized processing and coordination of all administrative, financial and regulatory matters as they relate to all research studies under the direction of the Vice President of Research and supported by the Directors of Clinical Research, and Basic and Translational Research, as well as the Director of Research Administration.

2. Determination, coordination and tracking of appropriate review of all research studies initiated involving Legacy patients or using Legacy facilities, sites, investigators or resources by the Senior Research Regulatory Specialist through the IRB. All research involving Legacy patients or using Legacy facilities, sites, investigators or resources is required to be submitted to Legacy IRB. A determination may be made that the proposed research does not, under some very limited circumstances, constitute Legacy being “engaged” in the research. However, the assumption is that the proposed research is to be overseen by LRI departments and functions. In the normal case, the LRI Manager of Clinical Research directs the internal administrative review, that includes legal contracts, budgets and logistics within involved clinical departments, to provide LH administrative leadership adequate feedback on which to base approval. Once an approved application is signed off by the responsible LH clinical administrator, initial IRB review takes place under the direction of the LH Policy 100.18.

3. Providing expert assistance as needed in the development, planning and execution of research projects or studies conducted within LH including specialists in research regulation, fiscal management and budgets, biostatistics, clinical research coordination and clinical outcomes research including registries. Clinical Research Coordinators from LRI can provide comprehensive management of a study, partial support of certain aspects of a study or, at the discretion of the Director of Clinical Research, not be involved.

4. Determining and, if necessary, providing logistical support in collaboration with the various hospital departments, clinical units and staff needed for conducting specific clinical trials and research studies at Legacy facilities with Legacy patients or resources.

5. Allocation of available institutional research resources, including funds, research equipment and space as they exist within LH as they are required for the execution of research under the direction of the Vice President of Research.

6. The allocation of institutional personnel resources in support of various research projects and studies under the direction of the Vice President of Research.

7. As Institutional Official, the Vice President of Research will determine whether it is feasible for Legacy Research Institute to manage and facilitate any research grants awarded to Responsible Staff.

IMPLEMENTATION PROCESS:

1. This policy will be implemented by coordination of the VP of Research, Directors of Clinical Research, Basic and Translational Research, and the Director of Research Administration.
2. Appropriate education and documentation within hospital departments will be instituted as required by specific studies.

Key Words: Research, Clinical Trials, Principal Investigator, Institutional Review Board
References: LH 100.18; LH

Approval:

Legacy Research.
Operations Team
MQ&C
Legacy Health Board of Directors

Originator: Legacy Research
Owner: VP of Research; Director of Research

ADMINISTRATIVE

Policy #: 100.84
Origination Date: 09/07
Last Revision Date: 10/22

SECTION: ADMINISTRATION & MANAGEMENT
TITLE: INTRODUCTION, PROCESSING AND TRACKING FOR MEDICAL DEVICES REQUIRING APPROVAL BY THE LEGACY INSTITUTIONAL REVIEW BOARD

FACILITY:

☒ Legacy Emanuel Hospital and Health Center
(as applicable: ☐ LEMC only ☐ RCH only ☐ Unity Center for Behavioral Health only)

☒ Legacy Good Samaritan Medical Center	☐ Legacy Medical Group
☒ Legacy Meridian Park Medical Center	☐ Legacy Urgent Care
☒ Legacy Mount Hood Medical Center	☐ Legacy Lab Services
☒ Legacy Salmon Creek Medical Center	☐ Legacy Visiting Nurse Association (Hospice)
☒ Legacy Silverton Medical Center	☒ Legacy Research Institute
☐ Administrative/System Support Services	☐ Other:

PURPOSE

The purpose of this policy is to ensure that all medical devices requiring approval by the Institutional Review Board are properly managed by the Research, Purchasing and Billing Departments. This includes Humanitarian Use Devices, 510(k) devices and Investigational Device Exemptions involved in clinical trials.

DEFINITIONS

Executive Value Analysis Committee: A committee comprised of Clinical Operations executives, senior medical professionals, senior finance executives, Supply Chain and Quality Assurance managers, chartered with final oversight and approval of new products, system-wide standards and their related safety, efficacy and budget related impacts.

510(k) Devices: A device that has been cleared for marketing by the U.S. Food and Drug Administration (FDA) that has been deemed “substantially equivalent” to a similar device that is already marketed. In some cases, manufacturers conduct small clinical trials on 510(k) devices to provide safety data and evidence of efficacy.

Humanitarian Use Device (HUD): A medical device that is intended to benefit patients in either the treatment and diagnosis of disease or conditions that affect fewer than 4,000 individuals in the United States each year. The FDA allows the marketing of HUDs with evidence of safety and probably

benefit, but they can only be used in facilities where an Institutional Review Board (IRB) provides oversight.

Institutional Review Board (IRB): A committee designated by an institution to review, prior to the initiation of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights, safety, and welfare of human subjects.

Investigational Device Exemption (IDE): An investigational device exemption allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support an application to the FDA

Post Approval Extension Study: A Post-Market Approval (PMA) Study is a clinical study or other investigation, usually conducted under a single protocol and included in the Pre-Market Approval order, to gather specific information to address precise study objectives about an approved medical device. Post-Approval Extension Studies represent an extension of a post-market approval study. For Medicare purposes, these studies use the PMA number assigned to the original FDA-approved post-market approval (PMA) study.

POLICY

A. Responsibilities

1. Legacy Research will work in collaboration with Supply Chain Management and Patient Business Services (Regulatory Compliance) to ensure the proper introduction, billing and tracking of medical devices used in clinical trials.
2. Supply Chain Management will work in collaboration with Legacy Research to provide information that is required for providing oversight of the use of these devices in clinical trials by the Institutional Review Board.

B. Legal Considerations

1. Legacy Research is required to provide information to the IRB regarding the management and use of medical devices in clinical trials by 21CFR50 and 21CFR812.
2. Supply Chain Management requires information to accommodate the orderly introduction, billing and tracking of medical devices utilized in clinical trials as required by 21CFR803 and 21CFR821.

PROCEDURE

I. Initial Introduction of a medical device to be used in an IRB approved activity in Legal Health (LH)

A. Investigator or physician requests IRB approval to utilize IDE, HUD, 510(k) or other medical device in LH.

B. Investigator or physician submits completed IRB packet to the Research Department.

C. The IRB, upon approval of the research, will issue an approval document, which the investigator may utilize to notify Supply Chain Management (SCM) and Patient Business Services (Regulatory Compliance) to coordinate the introduction of the device into the supply chain for purchasing, storage and use requirements.

D. Investigator will notify SCM and LH department managers of IRB approval by submitting the IRB approval document to SCM and to department managers where the device is to be used. Investigator will document notification to both SCM and Legacy Health department managers.

1. Executive Value Analysis Council (VAC) reviews and clarifies operational parameters of a device usage.
2. Upon VAC approval, SCM will proceed with New Product Introduction.

II. TRACKING DEVICES:

A. Investigator will provide Purchasing and Clinical Research Department with information consistent with Sponsor requirements to allow for proper tracking of IRB approved devices.

B. Investigator will arrange with Purchasing that research devices will be stored in a secured area with limited access. Investigator will ensure that research devices will **NOT** be stored in general areas where they can mistakenly be used for non-qualifying patients. Investigator will ensure that research devices are properly marked as research devices only.

C. Investigator will be instructed to notify the appropriate department manager, department business analyst, and Patient Business Services (regulatory Compliance) at time of procedure scheduling that an IRB approved device is being used.

D. Investigator will ensure that continuous device tracking information will be consistent with sponsor requirements and shall also include at a minimum the following:

1. Model/Lot/Serial number as appropriate
2. Lawson number
3. Date and time device received
4. Receiving location
5. Name of person receiving device
6. Date and time of device transfer to storage
7. Storage location
8. Name of person completing transfer

E. SCM/PBS will provide CRSS (Research) via email monthly documentation of use of IRB designated devices throughout all Legacy Health sites. This documentation will include at a minimum IDE or HDE number, date of service, physician provider, number of devices and patient account number.

Approval: Patient Business Services
Supply Chain
Operations Team

Originator: Research Department