

LEGACY HEALTH

ADMINISTRATIVE STANDARD

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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

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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. In addition, the Clinical Vice President of Research may approve an IRB authorization agreement that defers review to an external IRB.
5. 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 (1) 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** – 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.

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. Encourage continuing constructive communication between the IRB and the research investigator as a means of safeguarding the rights, safety, and welfare of human subjects.
 - d. 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.
 - e. 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 and the use or disclosure of protected health information ("PHI") for research purposes.
 - f. Maintain all documentation of informed consent, authorization and waiver of authorization as it pertains to research activities conducted within Legacy Health.
 - g. Have the right to disapprove the conduct of a research study in spite of IRB approval. However, Legacy Health may not approve a research study which the IRB has not approved.
 - h. Review requests for the retrospective review of medical records applying the minimum necessary requirements as set forth in 700.15 and in accordance with 700.17, Use and Disclosure of PHI Through Internal and External Data Registries/Repositories.
 - i. Review requests for the creation or establishment of Registries/Repositories as specified in Policy 700.17.

2. Legacy Research Institute ("Legacy Research") shall implement policies, rules, regulations and procedures for the proper safeguarding of the welfare of human subjects participating in all forms of research tests and evaluation at Legacy Health.
 - a. Maintain appropriate and informative records of the IRB's review of 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. Legacy Research, 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 statutes, regulations and common law precedents which may govern their duties and responsibilities hereunder through consultation with 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:
 - i. 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 not be effective for medical research studies at Legacy Health.
- 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. Legacy Health's Compound Consent and Authorization form can be found on the Legacy Internet – Research.
2. 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.
- a. 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.
 - b. 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.

- c. The authorization must be written in plain language.
 - d. Legacy Health will provide the individual with a copy of the signed authorization.
3. 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).

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4. 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.
 5. 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
HIPAA Registries Committee
Legal
Executive Council
LH Board

Originator: Legacy Research

ATTACHMENT 1

THE INSTITUTIONAL REVIEW BOARD (IRB)

1. Legacy Research 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 Clinical Vice President of Research. The term of appointment will be at least two years and may be renewed if deemed necessary or desirable. Outgoing members are encouraged to nominate their replacement. The Clinical Vice President of Research may veto any approval granted by the IRB. In turn, the Clinical 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, expedited review of protocols and informed consent and authorization forms, review of requests to use investigational drugs in emergency/life threatening situations, retrospective medical records reviews, registries/repositories and conducting the IRB meetings.
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, 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 shall consist of a minimum of ten members with six members constituting a quorum 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.
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 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 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 termination.
12. The IRB 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 Noninstitutional Investigator Agreement (NIA) 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.
16. The IRB Questionnaire, Consent Form Template and Data Use Agreement Template are located on the Legacy Internet – Research.

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.

Surveys are "exempt" from IRB review. An institution or sponsor may choose to have a survey reviewed by the IRB but generally that will be conducted only if the survey involves very sensitive subject matter.

Expedited review shall be conducted by the IRB chairperson or by one or more of the experienced IRB members designated by the chairperson to conduct the review.

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 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.

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 investigational 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 IND”.

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 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 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 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.

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.

ATTACHMENT 4

RETROSPECTIVE MEDICAL RECORD REVIEWS

When retrospective medical record review audits are conducted there are several issues to consider:

1. Confidentiality as it relates to institutional practices, specific physician practices and specific patient data, must be assured by the data collector.
 - a. Retrospective medical record reviews must be approved and conducted in accordance with 700.17, Use and Disclosure of PHI Through Internal and External Data Registries/Repositories.
 - b. Data gathering procedures must be carefully designed to ensure that only the minimum necessary information relevant to the project will be obtained per Legacy Policy 700.15.
 - c. Only a code or hospital number should be used - not the patient's name. Human subjects' names should not be disclosed to non-institutional affiliated parties. Use of patient initials and study number is to be encouraged whenever possible.
 - d. Subjects' names shall be stored in locked files.
 - e. Master codes and ciphers shall be kept in secure places, distinctly separate from encoded ciphered data.
 - f. Careful controls shall be kept on the shipment, delivery and transfer of all data, computer print-outs and files between offices and institution.
 - g. If information is gathered that could identify the patient then the investigator must first provide a justification for collecting that information and submit a plan detailing how and when that information will be de-identified.

2. What is the intent of the data collection?
 - a. Physician practice quality assurance data - does not require IRB review or approval.
 - b. Government agency - disease surveillance reports - does not require IRB approval.
 - c. Comparison of treatment modalities with intent to publish results requires IRB approval via expedited review process.