Human Research Protection Program Plan

1.1 Scope

This plan applies to all Pearl Institutional Review Board (IRB) staff. Throughout this document "Organization" refers to Pearl IRB, a commercial independent IRB.

1.2 Purpose

This Organization is committed to protect the rights and welfare of subjects in Human Research. The purpose of this plan is to describe this Organization's plan to comply with ethical and legal requirements for the conduct and oversight of Human Research.

This Organization's Human Research Protection Program (HRPP) is a comprehensive system to ensure the protection of the rights and welfare of subjects in Human Research. The HRPP is based on all individuals in this Organization along with key individuals and committees fulfilling their roles and responsibilities described in this plan.

1.3 Definitions

1.3.1 Agent

A person acting on behalf of Pearl IRB has the ultimate authority to determine whether someone is acting as an agent of this Organization.

1.3.2 Clinical Trial

A biomedical or behavioral research study of human subjects designed to answer specific questions about therapeutic interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices). Clinical trials are used to determine whether new therapeutic interventions are safe and effective.

1.3.3 Engaged in Human Research

An Organization is engaged in Human Research when its employees or agents are interacting or intervening with Human Subjects for the purpose of conducting Research. This Organization follows OHRP guidance on "Engagement of Institutions in Research" to apply this definition.

1.3.4 Human Research

Any activity that is either:

- "Research" as defined by DHHS and involves "Human Subjects" as defined by DHHS ("DHHS Human Research"); or
- "Research" as defined by FDA and involves "Human Subjects" as defined by FDA ("FDA Human Research").

1.3.5 Human Subject as Defined by DHHS

A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through Intervention or Interaction with the individual, or (2) information that is both Private Information and Identifiable Information. For the purpose of this definition:

- **Intervention** means physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private Information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
- **Identifiable Information** means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

1.3.6 Human Subject as Defined by FDA

An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen (identified or unidentified) a medical device is used.

1.3.7 Investigator

The person responsible for the conduct of the Human Research at one or more sites. If the Human Research is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator (PI).

1.3.8 Research as Defined by DHHS

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.[1] A "Systematic investigation" relevant to the Organization's research portfolio is defined as step by step methodical research, development, testing and evaluation, designed to develop or contribute to generalizable knowledge. "Generalizable knowledge" relevant to the Organization's research portfolio is defined as knowledge that could be applied to populations outside of the population served by the covered entity.

1.3.9 Research as Defined by FDA

Any experiment that involves a test article and one or more human subjects, and that meets any one of the following:

- Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
- Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

1.4 Mission

The mission of this Organization's HRPP plan is to protect the rights and welfare of subjects involved in Human Research that is overseen by this Organization.

1.4.1 Ethical Requirements

In the oversight of all Human Research this IRB follows the ethical principles outlined in the April 18, 1979 report of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research titled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," also known as "The Belmont Report":

- Respect for Persons
- Beneficence
- Justice

1.4.2 Legal Requirements

- This Organization commits to apply its ethical standards to all Human Research regardless of client funding source.
- Human Research must undergo review by the IRB. Activities that do not meet the definition of Human Research (e.g., most classroom activities, quality improvement activities, program evaluation, and surveillance activities) do not require review and approval by the IRB and does not need to be submitted to the IRB unless there is a question regarding whether the activity is Human Research.
- The Organization commits to apply the regulations of the DHHS relevant to the protection of Human Subjects.

[1] 45 CFR 46 102.d

- This Organization commits to apply the FDA regulations relevant to the protection of Human Subjects.
- Any questions about whether an activity meets the regulatory definitions of Human Research should be referred to Pearl IRB who will provide a determination.

1.4.3 Other Requirements

- When reviewing research that involves community based research, the IRB considers Community-Based Research Principles (i.e., http://www.washington.edu/research/main.php?page=communityPrinciples).
- The Organization prohibits review of Human Research conducted or funded by the Department of Justice (DOJ).
- When Human Research is conducted or funded by the Department of Defense (DOD), this Organization commits to apply the DOD Directive 3216.02, which includes the requirement to apply 45 CFR §46 Subparts B and D[2]. When Human Research is conducted or funded by the Department of the Navy, the Organization commits to apply SECNAVINST 39000.39D.
- When Human Research is conducted or funded by the Department of Education (ED), this Organization commits to applying 34 CFR §97 Subpart D (equivalent to 45 CFR §46 Subpart D), 34 CFR §98.3, 34 CFR §98.4, 34 CFR §356.3, and 34 CFR §99.
- When Human Research is conducted or funded by the Department of Energy (DOE), this Organization commits to applying the DOE O 443.1A and to use "Checklist for IRBs to Use in Verifying That HS Research Protocols Are in Compliance with the DOE Requirements."
- When Human Research is conducted or funded by, or when the results of research are intended to be submitted to or held for inspection by the Environmental Protection Agency (EPA), this Organization commits to applying 40 CFR §26, which includes the requirement to apply 45 CFR §46 Subparts B and D.

1.4.4 Sponsored Human Research

For both sponsored and non-sponsored Human Research; this Organization abides by its ethical principles, regulatory requirements and its policies and procedures.

1.4.5 Scope of Human Research Protection Program

The categories of Human Research overseen include:

- Forms of human research that do not include prisoners, non-living individuals, pregnant women, and neonates.

The categories of Human Research not overseen include:

- Research conducted outside the United States or its territories.

1.4.6 Human Research Protection Program Policies and Procedures

Policies and procedures for the HRPP are available on the following Web site: http://www.pearlirb.com/resources/forms.

1.5 Human Research Protection Program Components

1.5.1 Organizational Official

The Chief Operating Officer (COO) is also designated the Organizational Official (OO).

The COO has the authority to take the following actions or delegate these authorities to a designee:

- Suggest Appointments or removal IRB members requiring approval by the IRB Co-chairs.
- Determine what IRBs the Organization might partner with.

[2] Quick applicability table for DHHS Subparts:

	DHHS	DOD	ED	EPA
Subpart B	X	X		X
Subpart C	X	X		
Subpart D	X	X	X	X

- Approve and rescind partnership agreements with IRBs.
- Suggest the creation of policies and procedures related to the HRPP that are binding on the Organization. Institute regular, effective, educational, and training programs for all individuals involved with the HRPP.
- Ensure that the HRPP has sufficient resources, including staff appropriate for the volume and types of Human Research to be reviewed, so that reviews are accomplished in a thorough and timely manner. Resources will be reviewed, and adjusted by the COO if necessary, at least annually to ensure they continue to be adequate.
- Implement an auditing program to monitor compliance and improve compliance in identified problem areas.

- The IRB Co–chairs have the authority to take the following actions or delegate these authorities to each other:
    - Suspend research approved by the Organization.
    - Oversee the review and conduct of Human Research under the jurisdiction of the HRPP.
    - Periodically review this plan to assess whether it is providing the desired results and recommend amendments as needed.
    - Establish policies and procedures designed to increase the likelihood that Human Research will be conducted in accordance with ethical and legal requirements.
    - Ensure that the research review process is independent and free of coercion or undue influence, and ensure that officials of the Organization cannot approve research that has not been approved by the Organization.
    - Implement a process to receive and act on complaints and allegations regarding the HRPP.
    - Investigate and remediate identified systemic problem areas and; where necessary, removal of individuals from involvement in the HRPP.
    - Review and sign federal assurances (FWA) and addenda.
    - Fulfill educational requirements mandated by OHRP.
    - Report suspensions, terminations, and non-compliance to the federal government.

  Individuals who are responsible for business development, or any staff who has a personal or professional conflict of interest, are prohibited from carrying out day-to-day operations of the review process.

    - Space: Pearl IRB is based in Indianapolis, Indiana. The office space consists of multiple offices, conference room, kitchen and bath facilities.
    - Personnel: The IRB Co-Chair and IRB coordinator reside in the Indianapolis Office. All other IRB core and adjunct members are not located in the office space. All IRB members are connected via teleconference and email to conduct Board meetings, confer with clients and receive and document review of materials.
    - HRPP education program: The HRPP education program is a combination of internal SOPs, forms and checklists and outside resources such as NIH HRPP training, PRIMR training and other commercial training courses.
    - Legal counsel: Pearl IRB is represented by Alerding, Castor and Hewitt in Indianapolis, IN
    - Conflict of interest: Conflict of interest is rare as Pearl IRB does not conduct research. Conflicts are handled in accordance with the Board Membership. The company co-founders do not sit on the IRB. The COO oversees the quality system, but doesn't sit on the IRB.

- Quality improvement plan: IRB staff conduct continuous training for quality improvement. Annually the IRB staff train on SOPs. The IRB coordinator chooses training for the IRB on a quarterly basis to ensure continued education.
- Community outreach: When local issues are important to the review, the local community may be consulted.
- IRBs: Pearl IRB may rely on another IRB as outlined in the Cooperative Review SOP.
- The COO will review community outreach activities and the space and needs of the IRB on at least an annual basis. Weekly the IRB coordination team, which includes the COO, IRB Co-chair and IRB Coordinator, meets to review the workload and ensure that adequate staff are available. Adjustments will be made to the programs if necessary.

1.5.2 IRB

The IRB has the authority to:

- Approve, require modifications to secure approval, and disapprove Human Research. All Human Research must be approved by the IRB prior to initiation.
- Suspend or terminate approval of Human Research not being conducted in accordance with an IRBs' requirements or that has been associated with unexpected serious harm to subjects. The COO will be notified of all reports of non-compliance, unanticipated problems and suspensions and terminations.
- Observe, or have a third party observe, the consent process and the conduct of the Human Research.
- Determine whether an activity is Human Research.
- Evaluate financial interests of investigators and research staff and have the final authority to decide whether the financial interest and management plan, if any, allow the Human Research to be approved.
- Conduct continuing reviews of approved research. Review proposed amendments, adverse events, protocol deviations, and matters of non-compliance.
- Require research progress reports.
- Audit and/or monitor the research and researchers for adherence to the federal regulations and policies and IRB policies and procedures.

The IRB reviews research activities to ensure that:

- Risks to subjects are minimized;
- Risks to subjects are reasonable in relation to anticipated benefits;
- Selection of subjects is equitable;
- Informed consent is obtained or appropriately waived from all prospective subjects and documented;
- The research protocol includes a plan for data and safety monitoring, if applicable;
- Subjects' privacy and confidentiality are protected; and
- Appropriate additional safeguards are incorporated for specified vulnerable subjects.

Designated IRB members and IRB staff have the responsibility to follow HRPP policies and procedures.

1.5.3 Legal Counsel

Legal Counsel has the responsibility to:

- Provide advice upon request to the COO, IRB, and other individuals involved with the HRPP.
- Determine whether someone is acting as an agent of the Organization.
- Determine who meets the definition of "legally authorized representative" and "children" when Human Research is conducted in jurisdictions not covered by policies and procedures.
- Resolve conflicts among applicable laws.

1.6 Education and Training

Individuals who serve on Pearl IRB are to review this plan as part of initial orientation. The IRB is to conduct refresher training as needed to maintain awareness of this policy. IRB members, IRB staff, and others involved in the review of Human Research must complete a human subjects research training program. This training is valid for a two-year period, after which time a refresher course or additional training must be completed. IRB staff also train IRB members on the SOPs, checklists, and worksheets applicable to IRB members including regulatory and guidance requirements. Pearl IRB will enhance the understanding of participants, prospective participants, and communities by speaking about IRB functions, FDA and OHRP guidance at public meetings and forums on both a local and national basis. Public outreach is tracked in the presentations folder on the company server. Using the IRB Quarterly Metrics form, Pearl IRB obtains and evaluates feedback on their outreach activities to ensure continued improvement.

1.7 Quality Improvement in the HRPP

Scope of Quality Improvement Policy

The Quality Improvement program focuses primarily on reviewing and monitoring of the activities, policies, procedures, and records for the following groups:

- IRB
- IRB staff involved in HRPP education and outreach

Quality Improvement Policy Goals

The purpose of the HRPP Quality Improvement policy is to promote and verify the following:

- Integrity of HRPP activities
- Education and training of staff and IRB members
- Evaluation and follow-up of Quality Improvement initiatives and corrective actions and implementation of new quality improvement activities.
- Implement a Quality Improvement plan that periodically assesses the compliance of the HRPP.

Development and Review of Quality Improvement Activities

The IRB Coordinator or IRB Chair/Co-Chair is responsible for drafting proposals for HRPP Quality Improvement initiatives after review of the regulations, guidance, and findings from previous HRPP Quality Improvement projects, in consultation with the COO. The COO will review and approve HRPP Quality Improvement initiatives, as applicable, based on the scope of the activity (e.g., review of HRPP policies).

Implementation of Quality Improvement Activities

The IRB Coordinator or IRB Chair/Co-Chair is responsible for the implementation and communication of HRPP Quality Improvement activities. The COO and/or Institutional Official will set an effective date for implementation of new projects. When a HRPP Quality Improvement initiative represents a significant change to existing processes or practices, the effective date will be set to allow for communication, including education and planning for operational changes.

Quality Improvement Program Maintenance

The IRB Coordinator or IRB Chair/Co-Chair is responsible for maintaining the HRPP Quality Improvement program. The COO will review program findings and ongoing HRPP Quality Improvement initiatives as needed, at least annually. Specific findings from directed reviews will be forwarded to the IRB Chair, and/or to the IRB Coordinator. Program initiatives will be developed (as described above) and/or updated as HRPP needs are recognized or changed.

Quality Improvement Plan

Periodic Compliance Audit of IRB Minutes

Annually the IRB will complete an internal audit of the meeting minutes to ensure the regulatory criteria are documented. The IRB will rely on the Meeting Administration SOP for the list of

items to be included in the minutes. The annual report will be submitted to the convened IRB for discussion. Any non-compliance will need an action plan by the convened IRB to ensure regulatory criteria are being discussed.

IRB Member Evaluation

IRB members will be evaluated at least annually as stated in the Board Membership SOP.

IRB Performance Metrics

The IRB Coordinator or IRB Chair/Co-Chair produces periodic metrics and analysis of the IRB operations and functions, including measurements of processing times and activity volumes for the IRB and for each protocol event.

Continuous Quality Improvement

Based on the results of the assessments, the IRB will identify root causes of problems, develop, implement or recommend action plans to correct issues and provide education and outreach to promote effectiveness of improvements.

Based on the results of the assessments, the IRB will:

- identify root causes of problems
- foster the development of solutions
- implement or recommend appropriate courses of action
- provide education and outreach programs
- evaluate effectiveness of solutions/outcomes

Quality Indicators

- *IRB Member Evaluation*
- *Evaluation of IRB Minutes*

Efficiency Indicators

- *Processing Time for Applications*
- *Implementation of conditional approval determination*

Effectiveness Indicators

- *Implementation of SOPs*
- *Continuing upgrade of forms*

1.8 Questions and Additional Information for the IRB

The IRB wants your questions, information, and feedback.

Contact and location information is:

Pearl IRB Coordinator
29 E. McCarty Street Suite 100
Indianapolis, IN 46225
Email: info@pearlirb.com
(317)899-9341, extension 2

1.9 Reporting and Management of Concerns

Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the HRPP may be reported orally or in writing. Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to the Coordinator, IRB Chairs, or COO. The IRB has the responsibility to investigate allegations and findings of non-compliance and take corrective actions as needed. The COO has the responsibility to investigate all other reports and take corrective actions as needed. Employees who report in good faith possible compliance issues should not be subjected to retaliation or harassment as a result of the reporting. Concerns about possible retaliation should be immediately reported to the COO or designee.

Research staff, research subjects or any other person who has a question, concern, complaint, suggestion, request for information, or input regarding the Human Research Protection Program

(HRPP) may contact Pearl IRB. Any person who feels that they have been subjected to coercion or undue influence regarding aspects of human subjects research, or feels that they have observed issues of concern regarding human subjects research, may also contact the IRB. Any and all concerns, complaints, input, or suggestions regarding the HRPP and all allegations of coercion, undue influence or noncompliance are thoroughly investigated and, if applicable, corrective actions taken to rectify the situation. Ultimately, the COO is responsible to assure that all concerns, complaints, and allegations have been addressed appropriately and that input and suggestions related to the HRPP are considered when reviewing the program. General requests for information will be addressed by the IRB coordinator. If it appears that the concern/complaint could be an incident of noncompliance, or if the concern/complaint appears to involve an unanticipated problem involving risks to subjects or others, further inquiry will follow procedures delineated in the Unanticipated Problems and Non-Compliance SOP.

To make such reports or request information contact:
Pearl IRB Coordinator
29 E. McCarty Street Suite 100
Indianapolis, IN 46225
Email: info@pearlirb.com
(317)899-9341, extension 2

1.10 Monitoring and Auditing

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and organizational requirements will conduct periodic audits. Audits will focus on areas of concern that have been identified by any entity, i.e., federal, state or institutional. Random audits may also be conducted. Pearl IRB will assess the compliance of the HRPP on a periodic basis by auditing the IRB practice against its processes and Health Authority expectations. The goals of the quality improvement plan are to track and correct non-compliance. One objective will be to reduce the number of non-conformities. The second objective will be to ensure the HRPP meets the expectations of HHS. Measures of compliance will be adherence to SOPs, completeness of training files, and adherence to OHRP and FDA regulations. Compliance assessments may be conducted by non-board members, the COO or the Co-chair or coordinator. Improvements will be made by the addition of new or amended policies, procedures, checklists, or forms.

1.11 Disciplinary Actions

The IRB may place limitations or conditions on a study whenever in the opinion of the COO such actions are required to maintain the HRPP.

1.12 Approval and Revisions to the Plan

This HRPP Plan is to be approved by the COO. This plan is intended to be flexible and readily adaptable to changes in regulatory requirements. The COO has the responsibility to review this plan to assess whether it is providing the desired results. The COO has the authority to amend this plan as deemed necessary.

The COO, or a designee, will notify all IRB members via email if there is a change in the IRB HRPP Plan or IRB policies and procedures. All members must acknowledge and train on the updated documents before the member is eligible to perform a review for the IRB. If necessary, updated documents will also be published and/or replaced on the IRB website.

Approved:
Gretchen M. Bowker

Chief Operations Officer/Organizational Official
21 December 2016