Jaeb Center for Health Research

Human Research Protection Program Policy Manual

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VERSION HISTORY

The following table outlines changes for the HRPP Policy Manual:

VERSION NUMBER	AUTHOR	APPROVER	EFFECTIVE DATE	REVISION DESCRIPTION
1.0	Lesley Zajac	N/A	31 Dec 2013	Integrated the guidelines for JCHR implementation.
2.0	Tiffany Piquet	N/A	20 Jun 2014	Edits; clarified HRPP reviews; incorporated ethics training; provided supporting materials for the scientific review of research; incorporated compliance with state laws; added a section on the assessment of compliance; updated FCOI policies and procedures; updated policy on use of investigational drugs and devices; updates references to sponsor interactions; updates structure and composition of IRB; updated reviews of research; updated vulnerable populations; updated IRB documentation; updated ethical standards; updated compliance with laws and regulations
3.0	Tiffany Piquet	N/A	14 Sep 2014	Clarified assurance with the code of federal regulations; added definitions; clarified the process for maintaining resources to support the HRPP; provided examples of FCOI management strategies; updated policy on use of investigational drugs and devices; clarified IRB composition and membership rules; updated IRB evaluations of research protocols; added information regarding data safety monitoring plans; added section on protection of participant privacy; updated IRB waiver section; updated expedited reviews and exempt determinations sections; updated info on IRB minutes
3.1	Jennifer Neal-Jimenez	N/A	15 Feb 2015	Updated community involvement; clarified no research on pregnant women
3.2	Jennifer Neal-Jimenez	N/A	09 Mar 2017	Updated links to ensure proper functioning; other minor edits and reformatting
3.3	Jennifer Neal-Jimenez	N/A	19 Jun 2017	Clarification of primary reviews; other minor edits
4.0	Jeannie Perkins; Jasmine Conner; Kirra Meserve	Jeannie Perkins; [Reviewer-Mitch Drucker (IRB Chair)]	19 Jan 2018	Renamed; Reformatted; added table of contents and version history tracker; added the process for IRB requests for modifications per AAHRPP recommendation; updated emergency use; incorporate changes under the Final Rule (effective 01/19/2018) and updated policies and procedures accordingly: definitions, exempt research, continuing reviews, amendments, IRB responsibilities regarding UPs and Noncompliance, expedited research; approval criteria, continuing reviews; updated policies and procedures: reporting and managing undue influence, Human Subject Training; developed SOPs to transfer more procedural details to separate documents
5.0	Jeannie Perkins; Jasmine Conner; Kirra Meserve	Jeannie Perkins	24 Jan 2018	Reverted the following policies as the feds moved the effective date of the Common Rule changes to 19 July 2018, and so some provisions are not applicable under the current Common Rule: 2001.8/03 Continuing Review; 2010.10/02 Exempt Research; 2010.10/03 Expedited Research; 2017.12/11

VERSION NUMBER	AUTHOR	APPROVER	EFFECTIVE DATE	REVISION DESCRIPTION
				Request for Waiver/Alteration of Consent/HIPAA; 2017.12/12 Posting Clinical Trial Consent Forms; 2010.10/05 Approval Criteria.
6.0	Jeannie Perkins; Jasmine Conner; Kirra Meserve	Jeannie Perkins	01 Sep 2018	Included HHS registration; updated the assessment of compliance, quality and effectiveness of the HRPP and IRB; updated educational activities for research participants; updated reporting and managing noncompliance; updated allegations and finding of research misconduct; updated conflict of interest; updated public, private and industry sponsors; updated structure and composition of the IRB; updated IRB coverage; updated investigator qualifications; updated general application submissions for IRB review; updated methods of IRB review; updated approval criteria; added approval periods; added IRB requests for modifications; updated suspension and/or termination of research; updated IRB review of data and safety monitoring; updated protection of participant privacy interests; added assent and turning of age; added posting clinical trial consent forms; updated vulnerable populations; added addressing subject concerns, complaints or requests; updated IRB Documentation; added consent form signatures; other minor changes
6.1	Jeannie Perkins; Jasmine Conner; Kirra Meserve	Jeannie Perkins	15 Oct 2018	The Noncompliance Policy has been updated; clarified the review requirements of all members not assigned as primary or secondary for full board meetings in Section 2.13.1; clarified the timeline for completion of the minutes review checklist in Section 3.1.2.
6.2	Jeannie Perkins; Jasmine Conner; Kirra Meserve	Jeannie Perkins	16 Oct 2018	Clarified reviewer checklists, IRB requests for modifications, requests for waivers/alterations, consent form signature information, and clarified the system conversion date.
7.0	Jeannie Perkins; Jasmine Conner; Kirra Meserve; Jonathan Sibayan	Jeannie Perkins	21 Jan 2019	Addition of reference to Policy 2019.01/01 – Enrolling Family in Research; Reinstated the following updates per new final rule effective date of the Common Rule now on 01/21/2019 - Exempt Research and Expedited Research; Added the Transition Plan to 2018 Requirements under 45 CFR 46; Other minor edits; Updated Minutes Review Checklist Template
7.1	Jeannie Perkins; Kirra Meserve; Jonathan Sibayan; Zachary Duff	Jeannie Perkins	27 Aug 2019	Added IRB Coverage for Other Sponsored or Investigator-Initiated Research (including fee schedule); Edited Single Use Coverage by the IRB; other minor changes for clarity
7.2	Jeannie Perkins; Kirra Meserve; Jonathan Sibayan; Zachary Duff	Jeannie Perkins	07 Feb 2020	Updated contents to reflect the official title change from Director of the HRPP to Chief Research Compliance Officer; specified GDPR now covered under the Research Compliance Department as managed by the Research Compliance Committee and not individual officers; other minor edits

VERSION NUMBER	AUTHOR	APPROVER	EFFECTIVE DATE	REVISION DESCRIPTION
8.0	Jeannie Perkins; Kirra Meserve; Jonathan Sibayan; Zachary Duff	Jeannie Perkins	10 Feb 2020	Updated to incorporate information regarding research involving pregnant women or fetuses most notably in the newly added section “Research with Pregnant Women or Fetuses”
9.0	Jeannie Perkins; Kirra Meserve; Jonathan Sibayan; Zachary Duff	Jeannie Perkins	30 Jun 2020	Added policy regarding enrolling employees in a study; Explained process for potential HIPAA violations; Referenced revised HIPAA training; Clarified reliance provisions; Added Brazilian data protection regulations under GDPR references; Other minor edits; Minor updates to permission requirements for Research with Minors; Minor updates to HRPP Policy List references.

Contents

1. OVERVIEW

The Jaeb Center for Health Research (JCHR) was established in 1993 as a freestanding, nonprofit coordinating center for multi-center clinical trials and epidemiologic research relating to eye diseases and disorders, and diabetes. JCHR does not conduct research by enrolling and overseeing the care of human subjects directly, but rather contracts with Institutions to serve as the Sites where human subjects research is conducted (except instances of online registries and the like). In this capacity, JCHR has responsibilities for oversight of trial conduct and has functions similar to a Sponsor or contract research organization (CRO). In addition, consistent with its mission, in virtually all groups, JCHR is actively engaged in providing scientific direction with respect to formulation of study objectives, protocol development, statistical analyses, and manuscript writing.

The JCHR Human Research Protection Program (HRPP) was created in November 2013 with the primary purpose of protecting the participants in human subjects research by integrating all such activities, policies and procedures in which JCHR is involved. The Chief Research Compliance Officer (functioning as the "Director of the HRPP) is responsible for the management, implementation, and compliance of the HRPP at JCHR and for the oversight of the Site Investigators where the JCHR IRB is the IRB of record. The Chief Research Compliance Officer (CRCO)leads the JCHR HRPP under the umbrella of the Research Compliance Department. The CRCO must meet the minimum qualifications set forth by JCHR: a master's degree in related field with ten (10) years of clinical research experience required. At least ten (10) years' experience in regulatory compliance and/or management level experience in the research industry required. Must have certifications in research or be able to obtain necessary certifications as applicable (e.g., CCRP, CRCP, CIP, CIPP, etc.). The CRCO will pursue continuing education in human research protections, regulations, and related topics, and will lead continuing education for JCHR staff and IRB members in relation to human research protections in accordance with this manual, among other things.

The structure of this HRPP Policy Manual is in line with the standards established by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP). The JCHR HRPP has been accredited through the AAHRPP since 2015. As such, this manual sets forth JCHR HRPP and IRB policies to ensure compliance with federal regulations, guidance documents and guidelines, and is expanded through the use of Standard Operating Procedures (SOPs), Handbooks and Instruction Guides, and Other Resources. Therefore, the structure of the JCHR HRPP is as follows:

Federal Regulations
Guidance Documents & Guidelines
JCHR HRPP Policy Manual (Policies)
JCHR Standard Operating Procedures
JCHR Handbooks & Instruction Guides
Other Resources (Applications, Checklists, etc.)

This manual will identify the JCHR HRPP policy as established under applicable regulations or guidance, and will refer to specific SOPs to support compliance with said policies. Where federal regulations differ (as may be the case with the changes to 45 CFR 46 Subpart A, effective 21 Jan

2019, and the Food and Drug Administration's regulations), the most stringent requirement applicable will be implemented into JCHR policy, and subsequent SOPs. All JCHR HRPP staff (including the Institutional Review Board Staff) will be required to review and sign-off on this manual and SOPs through the JCHR Document Training Application. The IRB Members will be required to read and review this Manual and applicable SOPs and will sign a training form to attest to having read and understood their obligations therein. The Manual's policies and supporting SOPs have been translated into a handbook for the Investigators covered by the JCHR IRB, and each Investigator will be required to attest to having read and understood their obligations as described in the handbook (JCHR IRB Investigator Handbook). In addition, all applicable JCHR staff will be required to review and sign-off on the JCHR IRB Investigator Handbook based on their roles and responsibilities, as specified in the JCHR Training Matrix in JCHR SOP QM 104: Staff Training. This manual is publicly available through the JCHR Internet Webpage.

2. ORGANIZATIONAL STRUCTURE OF THE HRPP

2.1. JCHR Organizational Structure for the Protection of Human Subjects in Research to Ensure Autonomy and Accountability

The Executive Director is responsible for all scientific, legal, and financial activities of JCHR. These responsibilities do not include oversight of the Human Research Protection Program (the responsibility for which has been given to the CRCO) in order to avoid a conflict of interest, since the Executive Director serves as an investigator and/or Medical Monitor on certain protocols. Although the CRCO reports to the Executive Director, for the reasons stated above, the CRCO cannot receive any disciplinary action or be dismissed/terminated by the protection is in place to ensure that the CRCO is able to function independently to fulfill all responsibilities related to the protection of human subject and assurance of compliance, without fear of retaliation.

Currently, the CRCO heads the Research Compliance Department, which is the umbrella for the HRPP/IRB, the Research Compliance Committee and other Quality Assurance activities, such as conducting internal reviews of JCHR protocols under an IND or IDE known as "Internal Audits." These Internal Audits review the study-related conduct of JCHR staff, contractors and sites (as applicable) to ensure that compliance is maintained for JCHR led clinical trials. For more information on this process, please review the JCHR SOP QM 102: Internal Audits.

2.1.1. Non-HRPP Reviews and Resource Allocation to Protect Subjects

Prior to study selection, the JCHR Executive Director is responsible for development of the portfolio of projects with which JCHR will be involved. The initial assessment involves determining if the project has scientific merit and is consistent with JCHR's mission as a nonprofit clinical research organization. Assuming it does, then a feasibility assessment is made with respect to whether JCHR has the resources and personnel available for its intended role in the project. Many project collaboration requests are declined because the additional project could not be undertaken without compromising the time staff need to allot to existing projects. Thus, a critical element in deciding to take on a new project deemed to have scientific merit is whether there are staff available who will have sufficient time available for JCHR to conduct the research with a high level of quality.

When selecting sites and investigators, an assessment is made by the JCHR protocol team as part of an initial site evaluation/certification process of the site (including staff) and investigators in accordance with the JCHR SOP CT 204: Monitoring and Quality Assurance. Part of this process is ensuring investigator and staff knowledge of the protocol and corresponding procedures. Separate certification procedures are required for certain testing that is performed as part of a study. For studies that are more than minimal risk, an assessment is made as to whether the site will have the resources to care for the participant should a research-related injury occur.

While each protocol team is responsible for the development of its research protocols, most teams involve investigators at multiple sites and have some type of oversight committee that reviews and approves protocols for scientific and ethical merit before they are initiated. In some study teams, there are oversight review committees both internal to the team and external (meaning the reviewers are not Investigators or otherwise part of the team). Most protocols for which JCHR has involvement are funded fully or in part by a government or nonprofit granting agency, and as such, have an additional level of review conducted by the funding agency.

2.1.2. Scientific Reviews

Further, the Director (or Deputy Director) of Clinical Research Quality Assurance conducts a review of each protocol that includes an assessment of the protocol and related key documents, such as the informed consent form for scientific and ethical merit. This assessment is made to determine whether risks are being appropriately minimized such that research participants are not being unnecessarily exposed to risks and whether the risks are reasonable in comparison with the potential benefits of the research. In addition to the scientific review, this Director (or Deputy Director) reviews all grant awards and contracts with companies to assure that they are not in conflict with the protocol, JCHR's mission as a nonprofit company, and feasible to conduct. These reviews occur before the protocols can be submitted to the JCHR IRB. For more information on these reviews, please see the SOP CT 201: Clinical Trial Management Overview and General Principles. (NOTE: The JCHR IRB has additional requirements for the review of scientific merit as described in the corresponding section.)

2.1.3. HRPP Responsibilities of the CRCO

As stated, JCHR has delegated responsibility for the protection of human subjects to the CRCO (as the Director of the HRPP). The CRCO has the authority and the independence to manage and maintain the HRPP. The responsibilities of the CRCO include:

- Preparation and management of the annual HRPP budget
- Responsible for Financial Conflict of Interest compliance for all employees, independent contractors, IRB members, and JCHR IRB covered investigators
- Responsible for the review, investigation and reporting of Scientific Misconduct in Research
- Acts as the Research Integrity Officer
- Advises JCHR regarding the HIPAA Privacy Rule
- Advises JCHR regarding the General Data Protection Regulation (GDPR/LGPD) and compliance therewith

- Performs highly complex duties to facilitate the review and approval process of research activities, such as use of independent judgment in interpreting and applying relevant federal and state laws, regulations, and institutional policies and guidelines
- Instructs IRB chairs, members, staff, and researchers on special ethical topics
- Manages institutional and site compliance issues (in accordance with reliance agreements)
- Responsible for the institutional education activities related to ethical issues and the protection of the human subjects (the research compliance team also provides education activities to improve qualifications and expertise)

An organizational chart is available on the external JCHR website (under the Resources tab), showing the organizational structure within JCHR. (NOTE: Other organization officials do not have authority to approve research).

2.2. Covered Activities of the HRPP

Consistent with the description above, the HRPP is responsible for human subjects and related training, Financial Conflict of Interest, Research Misconduct, Undue Influence management, Noncompliance management, and the JCHR Institutional Review Board. Processes, definitions, criteria, applicable issues, and applicable materials are covered herein and/or under specific policies and procedures. These materials are intended to clearly delineate the ethical practices and standards of the JCHR HRPP and IRB respectively. Upon request, all of these policy and procedure documents are available to regulatory agencies, research sponsors, investigators, research staff, research participants, and JCHR IRB for viewing in the IRB Office and on the website (https://www.jaeb.org/hrpp/).

Under the policies established by the JCHR HRPP and consistent with 45 CFR 46 and 21 CFR 56, the JCHR IRB will review all human research activities designed or conducted at the JCHR. Accordingly, the JCHR IRB has assured federal regulatory agencies that the institution will review and approve all research that meet the federal definition of human subjects research.

2.2.1. General Data Protection Regulation (GDPR/LGPD) Activities

Under the requirements established by the European Union's General Data Protection Regulation ("GDPR") as of 25 May 2018, and by Brazil's Lei Geral de Proteção de Dados (or "LGPD") with a scheduled effective date of 15 August 2020, HRPP activities related to the data processing of qualifying data subject, or in coordination with European Economic Area (EEA) and/or Brazilian companies, compliance will be managed by the Research Compliance Committee. For more information on the functions of the Research Compliance Committee and GDPR/LGPD processes and procedures, see the SOP HRPP 607: General Data Protection Regulation Operations.

2.3. Registration of the JCHR IRB

The JCHR IRB is registered with the department of Health and Human Services (HHS) and has received and maintains a Federalwide Assurance (FWA) therein. Updates and reports are made

to HHS by the CRCO as required. Verification of JCHR IRB's registration, as well as any IRB's registration, can be found using the following link: https://ohrp.cit.nih.gov/search/search.aspx?styp=bsc. Our Institution/Organization name is listed as "Jaeb Ctr for Hlth Rsch" and our IORG Number is IORG0000451 for reference.

2.4. Transition Plan for 2018 Requirements of 45 CFR 46 (Federally Funded Research)

Federally funded research for which IRB review was made and the research was either waived, exempted, or approved pursuant to 45 CFR 46 of the pre-2018 Requirements (before January 21, 2019) will not be transitioned to, or required to comply with, the "2018 Requirements" which became effective 21 January 2019.

Federally funded research for which IRB review and final determination is made (waived, exempted, or approved with no changes required) on or after 21 January 2019 must comply with the "2018 Requirements."

Federally-funded research which is subject to the "cooperative research" provision of the "2018 Requirements" at 45 CFR 46.114(b) will be subject to the single IRB of record requirement as of January 20, 2020, unless the research qualifies for an exception as set forth in 46.114(b)(2).

JCHR has implemented the updated requirements to the consent template, as set forth in the 2018 Requirements, as those requirements do not conflict with the prior requirements or with FDA requirements. In general, JCHR anticipates that the "broad consent" for research conducted using Identifiable Private Information or Identifiable Biospecimens will not be in use at JCHR, as JCHR does not interact directly with patients or have direct access to information that constitutes "Private Information", as that term is defined in the 2018 Requirements. Rather, JCHR receives biospecimens and data from institutions that have either already obtained consent, have received a waiver of consent, or have removed Private Information and identifiers from the biospecimen or data. Should JCHR's practice change, JCHR will revisit the determination regarding implementation of broad consent.

In certain situations, JCHR may engage in research which requires the sharing of data or materials with other scientists. For example, NIH research policies customarily require that data or materials developed under NIH grants be made available to other scientists. In such situations, JCHR will require that the informed consent form(s) advise potential study participants of such requirements, and individuals may not participate in the study unless the individual agrees to the data and material sharing requirements as specified in the consent form ("Future Use"). While the data and materials (such as optical coherence tomography "OCT" images) might be identifiable if connected with Private Information, the data and materials are not provided to other scientists with identifiers such as name, medical record number, or similar information.

2.5. Activities Overseen under the HRPP

The Jaeb Center for Health Research (JCHR) maintains and follows written policies and procedures to determine when research activities must be overseen by the Human Research Protection Program (HRPP). These policies and procedures may be determined and maintained

by the Institutional Review Board (IRB) under the oversight of the HRPP. The JCHR IRB will review all human research activities designed or conducted at the JCHR.

The JCHR IRB has assured federal regulatory agencies that the institution will review and approve all research that meet the federal definitions of human subjects research as described below. Determining whether or not an activity meets the federal definition of human subjects research is a process. The definitions below will help the Investigator understand if IRB review is required.

According to the FDA regulations, a ***Clinical Investigation*** (i.e., "Research") is "any experiment that involves a test article and one or more human subjects…" and that essentially meets the requirements for Food and Drug Administration submissions or exemptions (21 CFR 50.3(c), 21 CFR 56.102(c)).

Under these FDA regulations, ***Human Subject*** means "an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject might be either a healthy human or a patient" (21 CFR 50.3(g)) and (21 CFR 56.102(e)).

However, 45 CFR 46 Subpart A (as applicable to any research regulated by a Federal department or agency) defines ***Research*** as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge."

The JCHR IRB is using the definition of 45 CFR 46 ("2018 Requirements") whereby ***Human Subject*** means "a living individual about whom an investigator (whether professional or student) conducting research:

- 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"

Also under the "2018 Requirements" for 45 CFR 46, ***Intervention*** "includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes", and ***Interaction*** "includes communication or interpersonal contact between investigator and subject."

2.6. JCHR Institutional Review Board Autonomy for the Protection of Human Subjects

The IRB is the only JCHR entity that is allowed to approve research activities, and it functions autonomously and independently from any other JCHR entity to ensure the protection of research participants. The JCHR has granted the IRB the authority to:

- approve, require modifications to secure approval, and disapprove all research activities overseen and conducted by JCHR (including sites submitting for coverage under the JCHR protocol)
- suspend or terminate IRB approval of research not being conducted in accordance with the IRB's requirements, or that have been associated with unexpected serious harm to participants, and

- observe, or have a third party observe, the consent process and the conduct of the research

JCHR takes all necessary precautions to ensure that research involving human participants does not commence until the research has received all approvals required by the JCHR IRB. Furthermore, as stated above, JCHR IRB has the sole authority to approve research as JCHR seeks to embody a culture of compliance. Researchers, research staff and HRPP staff receive continuing education reflecting this requirement. Also, the majority of the funding agencies will not release the funds unless IRB approval is received.

2.7. Reporting and Managing Undue Influence

The HRPP has established a policy regarding the reporting and management of attempted, or actual, undue influence of the IRB Members and/or any other HRPP or IRB staff. The policy states: "Any attempt or instance of undue influence of the IRB must be reported to the CRCO. The term "undue influence" refers to interference with the normal functioning and decision-making of the IRB as well as any other HRPP component. Furthermore, JCHR IRB classifies influence on an IRB member or HRPP staff member outside of routine processes in order to ensure a particular outcome as "undue influence". Any individual who is aware of an attempt or instance of undue influence related to the operation of the IRB or other HRPP component must report the incident" (HRPP/IRB Policy Number 2014.06/03). For more information on the process for reporting and managing Undue Influence, please review the SOP HRPP 601: Reporting and Managing Undue Influence {LINK}.

2.8. HRPP Education Initiatives

The HRPP is responsible for developing education and training programs for investigators, research staff, and IRB members to ensure the protection of the rights and welfare of research participants and to improve and maintain the level of expertise of the individuals responsible for protecting those rights.

The JCHR Federalwide Assurances (FWA) includes the responsibility of ensuring that investigators engaging in federally-conducted or -supported human subjects research understand and act in accordance with the requirements of the regulations for the protection of human subjects. As such, the Office of Human Research Protections (OHRP) strongly recommends that institutions and their designated IRBs establish training and oversight mechanisms (appropriate to the nature and volume of their research) to ensure that investigators maintain continuing knowledge of, and compliance with specific concepts. These concepts include the following: relevant ethical principles, relevant federal regulations, written IRB procedures, OHRP guidance and other applicable guidance, state and local laws, and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that investigators complete appropriate institutional educational training before conducting human subjects research.

To fulfill these training requirements and the requirements set forth by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA), the JCHR HRPP has established a policy that adapts these requirements to ensure that all Investigators and applicable JCHR staff are qualified to perform their roles and responsibilities as such. The Human Subjects Protection

Training Policy states, “In accordance with the federal regulations, the JCHR HRPP requires all investigators working on JCHR studies and all applicable JCHR staff to have adequate Human Subjects Training. In addition, the JCHR HRPP requires that investigators, research staff, and applicable JCHR staff have additional training in the principles of Good Clinical Practice per regulatory requirement” (HRPP Policy Number 2011.04/02). For more information on the training process and requirements, please see the SOP HRPP 602: Human Subjects Protection Training {LINK}.

2.9. Adherence to Applicable Local Laws and Regulations

When applicable, the following Florida Statues will be enforced and applied prior to the approval of human research in accordance with the SOP HRPP 603: Florida Laws and Regulations Applicable to Research {LINK}. The Reliance Agreements made with local institutions are required to capture local context information which includes, among other things, notifying the JCHR IRB of any applicable local laws or regulations that apply to research in the area in which they will be conducting the research activities. In addition, the IRB Administrator and the External IRB and Reliance Specialist have access to a state-by-state research related laws resource guide. All initial approvals of subject materials (e.g., consent forms) will be in accordance with Florida State Laws, but site-specific materials will be amended to reflect local laws applicable to the state in which the research will be conducted.

2.10. Resources of the HRPP

JCHR ensures that the HRPP has sufficient resources at its disposal to be able to carry out its duties with respect to the rights and welfare of research participants in the research activities conducted by the JCHR. Those resources include:

- Adequate staffing
- Adequate office and meeting space
- Access to outside consultants to provide additional expertise if needed
- Access to Spanish translation resources and other languages as needed
- Access to equipment and technology necessary to conduct and maintain a web-based IRB system
- Access to the necessary programming and web development expertise to ensure the optimal efficiency in the web-based system
- Access to adequate budgeted financial resources

The process by which JCHR maintains adequate resources for support of the operations of the HRPP is as follows:

- In the fourth quarter of each year, the CRCO and the Chief Operating Officer review the HRPP budget and actual spending for that year and determine recommended budget levels for the coming year
- This includes a review of staffing levels and the budget needed to manage the IRB
- The administrative staff of the Institutional Review Board then review the proposed budget and suggest any recommended changes or additions
- The CRCO reviews the final budget proposal with the Chief Operating Officer
- The final budget for implementation and inclusion within the general administrative (overhead) budget is approved by the Chief Operating Officer

- Throughout the year the budget is also reviewed by the CRCO against actuals on an ongoing basis and adjustments are made as necessary

2.10.1. HRPP Budget Components

The HRPP budget is a comprehensive part of the general administrative (overhead) budget. The overhead budget is established in January of each year and re-evaluated throughout the year on an ongoing basis. This evaluation of specific resources needed for the HRPP to function include the following:

- Space – Encompassing all facilities including office space, telephone system, and technology (including the web-based IRB management system)
- Personnel – To ensure that HRPP has adequate staff coverage
- HRPP Education Program – These resources are built from the space and personnel resources allocated under the budget
- Legal Counsel – Access to outside legal counsel is provided on an as-needed, as-requested basis and is a line item in the budget. JCHR does not have in-house legal advisors on staff
- Conflict of Interest – These resources are built from the space and personnel resources allocated under the budget
- Quality Improvement Plan (QIP)– These resources are built from the space and personnel resources allocated under the budget
- Community Outreach – Any resources needed in support of the community outreach activities are evaluated on an ongoing basis throughout the year
- Institutional Review Board –The budget includes such line items as meeting expenses, materials provided to the IRB members including educational materials, stipends paid to the IRB members and IRB Chair, memberships for CRCO and IRB Administrative staff in appropriate professional organizations, travel for CRCO and/or IRB Administrative staff to appropriate professional meetings or educational symposiums, office supplies, telephone costs, and postage

2.11. Transnational Research

The JCHR IRB does not plan to oversee research conducted outside of the US as it can pose some unique risks, specifically concerning the political, cultural or economic conditions of the research site. This type of research is commonly used for the pharmacological mega-trials that execute worldwide protocols. Therefore, the JCHR HRPP/IRB Policy states "JCHR IRB does not provide coverage for transnational research. Internet-based studies do not have boundaries, so they are not considered transnational. If the need for either arises, the JCHR will follow the International Conference on Harmonization/Good Clinical Practice (ICH/GCP) guidelines along with local laws and regulations" (HRPP/IRB Policy Number 2014.06/04). It is important to note that certain IRB xForms do ask about international involvement solely for tracking by the CRCO to ensure that the Research Compliance Committee is receiving applications for qualifying studies as they should.

2.12. Standards of Conduct

All members of the JCHR research community (IRB members and Chairs, IRB staff, the organizational official and employees) are obliged to follow the ethical principles of beneficence, justice, respect for persons, privacy, and confidentiality to govern the conduct of research involving human participants.

Beneficence: An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

Justice: An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of different circumstances or characteristics similarly.

Respect for persons: An ethical principle discussed in the Belmont Report requiring that individual autonomy be respected and that persons with diminished autonomy be protected.

Privacy: Control over the extent, timing, and circumstances of sharing oneself physically, behaviorally, or intellectually with others.

Confidentiality: Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

2.13. Organizational Response to Questions/Concerns of Research Participants

2.13.1. Research Participant Access to Information and/or Advice

JCHR maintains written policies and procedures to ensure that current, prospective and/or past research participants or their designated representatives have a reliable and confidential process allowing them to contact a knowledgeable and informed individual at the IRB Office, who is not affiliated with the research protocol, when they have questions, problems or concerns related to the research. This contact information is included in the Informed Consent Templates and on the JCHR public website (https://www.jaeb.org/hrpp). The CRCO is responsible for providing adequate and timely responses to these inquiries, and may consult with the IRB members, IRB staff, the sponsor, or site as necessary (e.g., someone contacts CRCO to find out who to contact to enroll in a study, and so the Director will put that person in touch with someone on the study team). Each communication will be documented and saved by the CRCO in a redacted manner.

2.13.2. Educational Activities for Research Participants

Given the nature of the research conducted by JCHR, such that study participants are not seen at JCHR, the involvement of community members in the design and implementation of the research activities and the dissemination of the results to the local community is not applicable. The main outreach for JCHR will be via the Research Participants tab on the JCHR public website (https://www.jaeb.org/hrpp). Through this website, potential participants and others can access information about research, research participation, and utilize quick links to relevant resources to

get more information. The HRPP Office will review the website and any available metrics to evaluate this outreach initiative.

2.14. Organizational Compliance, Quality and Effectiveness Auditing

2.14.1. Assessment of Compliance, Quality and Effectiveness of the HRPP and IRB

The initial assessment of the Human Research Protection Program and its components was done with the AAHRPP Accreditation Process during 2014/2015. Additionally each year, the Research Compliance Department (which includes the CRCO) reviews certain processes and procedures of the HRPP and IRB to establish that it is in compliance with regulations, and JCHR policies and procedures. This is conducted as part of the JCHR Annual Research Compliance Review and includes the reporting and management of conflicts of interest, noncompliance, SAEs, unanticipated problems, and exempt determinations among other things. Information collected for the review will be assessed with the Research Compliance Department to determine if process and procedures are clearly established and being followed with adequate documentation. Based on this review, plans of corrective actions may be prepared, and policies and procedures may need to be updated.

In addition, a sample of the IRB Meeting minutes will be evaluated no less than once a year in accordance with the IRB Meeting Minutes Review Checklist template {LINK}. Overall, this review is attempting to ensure that the research being reviewed and the determinations being made by the JCHR IRB, as demonstrated through the IRB Meeting Minutes, must be in accordance with the requirements of IRB Meeting Minutes as described in US Federal Regulation. In addition, standardization with Good Clinical Practice as promulgated by the FDA is expected, along with compliance of JCHR SOPs and policies and procedures. Further, the JCHR Human Research Protection Program (HRPP) is accredited through the Association of Accreditation of Human Research Protection Programs (AAHRPP) and so must be compliant with the AAHRPP standards. The checklist will be completed annually with a sample of meeting minutes (e.g., one meeting from each quarter).

2.14.2. Ability of Researchers and Research Staff to Comment on HRPP

The HRPP values open communication with investigators under its oversight. In order to protect human research participants and improve the effectiveness of the HRPP and the IRB, timely and appropriate responsiveness to their questions, concerns, and suggestions is essential.

As noted above, the JCHR internal website includes instructions on how to contact the HRPP and the IRB with comments, questions, concerns, and suggestions. Contact information is also listed on the public website (www.jaeb.org/hrpp). Information on the HRPP also is included in the monthly staff newsletter. HRPP staff also have the ability to attend project meetings and other less formal gatherings in order to discuss issues with staff and investigators.

2.15. Reporting and Managing Noncompliance

An important function of an institution's policies and procedures on serious or continuous noncompliance is to inform the research members of the institution on the institution's policies and procedures for responding to allegations of such noncompliance in accordance with the

JCHR HRPP/IRB Policy 2001.08/07 Deviation Reporting and Noncompliance as specified in the SOP HRPP 604: Noncompliance {LINK}.

JCHR has granted the responsibility for review of all human subjects research conducted in the US to the JCHR HRPP. The investigators are responsible for conducting the approved research in accordance with the IRB's requirements, as well as in accordance with all ethical standards, study policies, and federal or state laws or regulations applicable to the research study. It is the obligation of the investigators to submit a written report to the IRB regarding any significant deviations relating to research involving US Citizens, and then the IRB will report identification of those deviations as serious or continuous noncompliance to the CRCO. Significant deviations relating to the ethical standards and regulations of research with non-US Citizens, will be reported to and managed by the JCHR Research Compliance Committee (RCC), specifically as it relates to the General Data Protection Regulation (GDPR/LGPD) for the European Economic Area and Brazil respectively. For more information about compliance with the GDPR/LGPD, please see SOP HRPP 607: General Data Protection Regulation Oversight.

Serious or continuous noncompliance may pose an increase in risk to participants, adversely affect the welfare, rights, and safety of the research participants, or negatively influence the scientific study integrity. Willful violations of federal regulations and/or policies also may be indications of serious or continuous noncompliance.

In the event of serious or continuous noncompliance, or a qualifying breach, the CRCO will be required to report the event to the OHRP, FDA, and other regulatory agencies, as applicable. Additional reporting may need to be done for local institutions under the terms of a Reliance Agreement. (NOTE: An overview of the IRB's responsibility is also described in the applicable IRB responsibilities sections below.)

2.16. Allegations and Findings of Research Misconduct

In accordance with federal regulation, JCHR has established a policy for the handling of allegations and findings of research misconduct under the JCHR HRPP/IRB Policy 2017.12/14 Research Misconduct as described in the JCHR SOP HRPP 605: Research Misconduct {LINK}. The main responsibility for the receipt, evaluation and investigation of allegations of research misconduct and reporting of investigational findings falls to the CRCO as Director of the HRPP. Once the decision has been made to conduct an investigation, the IRB will be notified. Further, once the investigation has been completed, a copy of the official report will also be sent to the IRB for review. The IRB members will determine if IRB coverage will be suspended or terminated for any JCHR investigators or clinical sites/investigators in cases where the IRB is providing coverage for clinical sites. The Director of the HRPP will be required to report suspension or termination of research activities to the OHRP, as applicable. In addition, the FDA and funding agencies have specific reporting requirements. Further, in accordance with the Reliance Agreements established with local IRBs, the JCHR IRB may also need to report to the local IRB.

2.17. Conflict of Interest Policies and Procedures

Per JCHR HRPP/IRB Policy 2017.01/04, and in accordance with applicable regulations, JCHR must ensure that the design, conduct, and reporting of research is free from bias resulting from conflicts of persons involved in research conducted by JCHR. This is demonstrated through the establishment of an SOP detailing the training, disclosing, managing, and reporting of conflicts of interest (COI).

For JCHR employees, conflicts that meet reporting requirements must be reported at the time of hire (or acceptance of appointment for IRB members), annually, and any time there is a new or substantive change in these interests. COI training must occur no less than every four (4) years and whenever the COI policy or SOP are revised with major changes.

The policy applies to JCHR as an organization, JCHR employees, independent contractors, and IRB members. Certain aspects of the policy apply to research investigators from other institutions that are receiving funding through JCHR from a Public Health Service (PHS) grant for which JCHR is the grantee, or are receiving Institutional Review Board (IRB) coverage by the JCHR IRB. Additionally, this SOP covers situations where JCHR is the holder of an IND or IDE for a study or is delegated this responsibility by a study sponsor. For more information, please see the JCHR SOP HRPP 606 – Conflict of Interest {LINK}.

2.18. Use of Investigational or Unlicensed Drugs and Devices

Research participants are not seen at JCHR and all use of drugs and devices in protocols are at external sites. JCHR staff involved in the monitoring of a protocol must maintain accountability of drugs and devices in accordance with regulatory requirements and guidance documents as described in the JCHR SOP CT 205 – Investigational Product Accountability.

Per the following legal and regulatory requirements (21 CFR 312 and 21 CFR 812), JCHR principal investigators are responsible for determining whether an Investigational New Drug (IND) or Investigational Device Exemption (IDE) is required for a protocol. If an IND or IDE application is required, the principal investigator cannot proceed with a protocol until the corresponding submission has been provided to the FDA.

In cases involving a drug in which an IND has not been obtained or a device without an IDE because the principal investigator deemed it unnecessary, it is the prerogative of the IRB to request that the investigator obtain a formal review by the FDA to determine whether or not an IND/IDE is required. In such cases, review of the protocol will be deferred until the FDA ruling is received.

During the administrative review of submitted applications to the JCHR IRB, the IRB staff will verify the below:

- Test article has an IND or IDE or meets the exemption
- Confirms the IND or IDE number is valid

2.18.1. Investigational New Drugs

In accordance with 21 CFR 312.3, for protocols for which an IND is required, the JCHR principal investigator must provide the FDA IND Number on the application for IRB review.

The investigator cannot enroll participants until this is provided. When following FDA regulations and the research involves the use of a drug other than the use of a marketed drug in the course of medical practice, the following applies:

- The protocol use of a drug has an IND; or
- The protocol meets one of the FDA exemptions from the requirement to have an IND.

2.18.2. Investigational Device Exemptions

For protocols for which an IDE is required, the JCHR principal investigator must provide the FDA IDE Number on the application for IRB review. As stated within 21 CFR 812, there are three types of device studies: significant risk (SR), nonsignificant risk (NSR), and exempt studies. The Principal Investigator makes the initial risk determination.

The IRB must review this and is required to determine the device risk for investigation as a non-significant risk (NSR) device study or significant risk (SR) device study. The responsibilities of the IRB for such determinations are found in 21 CFR 812.66. When determining risk, the JCHR IRB considers both the potential harm of a protocol procedure, and by the device.

The definition of a SR device study can be found in 21 CFR 812.3(m) whereas the FDA does not specifically define an NSR device study. Studies indicating SR devices are those in which a potential for serious risk to health, welfare, and safety of the participant exists. NSR's should not be mistaken with minimal risk as they are two separate thresholds. For example, a study may be a non-significant risk device study, but could still be considered greater than minimal risk. The IRB serves as the FDA's surrogate concerning NSR investigations including but not limited to initial and continuing review.

Non-significant risk device studies are subject to abbreviated IDE requirements. An IDE submission is not required under the abbreviated requirements, but the requirements for labeling, informed consent, monitoring, records and reports, and promotional practices contained in FDA regulations still apply (ref. §812.2(b)).

At times, a device may be initially labeled as NSR, but it may be determined that the protocol constitutes a SR device study. If the IRB determines that an investigation is a SR device study, initially presented by the investigator as NSR, the IRB reviewer will defer to full board and the IRB will notify the JCHR/Sponsor investigator immediately of the SR determination. If the device protocol is determined to be a SR device study, the JCHR/Sponsor may not proceed with the protocol except under 21 CFR 812.30(a) which requires FDA approval of an IDE application. Further, the JCHR IRB's risk determination for all NSR/SR device protocols is documented in the corresponding IRB reviewers' checklist (and convened meeting minutes for full board) and this information is conveyed to the principal investigator in the decision letter.

2.19. Public, Private and Industry Sponsors

The written agreement for public funding and private nonprofit funding of research grants generally comes in the form of a "Notice of Award" from the funding agency and these typically are non-negotiable. Therefore, AAHRPP Standards under I-8, may not apply (as noted within the Contract Language Checklist). JCHR negotiates Clinical Research Collaboration Agreements (or

similar instruments) with industry sponsors who provide funding for a JCHR project. As defined in 21 CFR 50.3, a sponsor is a person or entity that initiates but does not actually conduct research. Rather, the sponsor distributes the drug or device to investigators and physicians for usage in clinical trials. The sponsor assumes responsibility for investigating the new drug or device, which includes compliance with applicable laws and regulations. For instance, a sponsor is responsible for obtaining FDA approval to conduct a clinical trial and for reporting the results to the FDA.

For verification purposes, the JCHR IRB requires that the JCHR principal investigator review the contract and funding agreement for each protocol to ensure the required language is included. This may be delegated to the contracts department in accordance with their contracts review under the Elements of Standard Contracts standard operating procedure). All JCHR contract specialists working on the contracts on behalf of JCHR are required to train on and use the JCHR SOP GC 701 – Elements of Standard Contracts when developing contracts.

3. INSTITUTIONAL REVIEW BOARD

3.1. Structure and Composition of the IRB

3.1.1. IRB Roster and Membership

Per HRPP/IRB Policy Number 2011.01/01, the Federal regulations require that membership of each IRB Committee include at a minimum, five members, with varying background and diversity among members. The committee shall comprise of one member whose primary concerns are in scientific areas, one member whose primary concerns are in nonscientific areas, and at least one individual not affiliated with the JCHR. IRB Members may serve on one or multiple JCHR IRB Committees, and may or may not be assigned expedited reviews based on their qualifications.

IRB Members are appointed by the Director of the HRPP in consultation with the IRB Chairs. Each committee will have at least one Chair and may have Vice Chair(s). Membership terms are for four years. IRB Members from one committee may serve as alternate members for another committee, given that the alternate has comparable qualifications. For example, a community-based participant advocate could serve as an alternate for another community-based participant advocate on another committee.

The Director of the HRPP appoints the IRB Chair(s) and IRB Vice-Chair(s). All IRB members, including IRB Chair(s) and Vice-Chair(s), are evaluated annually using an evaluation form, in accordance with JCHR HRPPP/IRB policies. The evaluations are completed by the IRB Office and the evaluation results are provided to the Director of the HRPP and the IRB Chair(s) for review. Written feedback will be provided to each IRB member, and each member is encouraged to respond/comment on the form. Details of each member of the JCHR IRB Committees can be found on the IRB Rosters as well as the JCHR Intranet.

3.1.1. New IRB Members

The current committee members may recommend a new member for the committee, and the IRB Administrator will inquire as to whether the individual is interested and if yes, request a resume/CV, which will be forwarded to the IRB Chair and the Director of the HRPP for review. Once the new committee member has been chosen, the following items are completed and the documents are submitted to the IRB Administrator: Conflict of Interest Disclosure form, JCHR IRB Member Training Acknowledgement form, GCP Training Certificate, HRPP's Policy Manual Training form, and payment information (if applicable).

The JCHR IRB is organized and overseen by the JCHR HRPP. The HRPP is led by the Director of the HRPP and reports directly to the Chief Operating Officer. The JCHR IRB office consists of the IRB Administrator and additional IRB Staff. Job Descriptions and CVs are available upon request.

3.1.2. IRB Member Assignment

In accordance with HRPP/IRB Policy Number 2013.01/01, the IRB Administrator will instruct the IRB Coordinator(s) to assign a primary reviewer to each application that will be reviewed. For every lead study application that will be assigned to full board review, a secondary reviewer will also be assigned. In the event that the primary reviewer is unable to lead the review and

discussion (i.e., personal emergency), the secondary reviewer will be able to serve as the lead to ensure that applications are not postponed due to no fault with the submission. When both the primary and secondary reviewers are present, then the secondary reviewer will focus on where there is disagreement with the primary reviewer or additional comments to support the primary review. Certain submissions that are initially submitted for expedited review and then are brought before the full board for discussion due to safety concerns (i.e., Site Addition to Protocol xForms, Miscellaneous Submission xForms, etc.), will not require a secondary reviewer.

Further, all members are expected to review the application (most appropriate for scientific members) or the consent forms (most appropriate for participant advocates) at a minimum, but all materials are available for review before, during and after meetings for all members via the Jaeb.my.IRBManager.com platform. Primary and secondary reviewers will need to be prepared to provide a summary of the application and lead the discussion for the committee. All members will need to be prepared to participate in the discussion of every submission, unless the member chooses to abstain. Certain submissions that are initially submitted for expedited review and then are brought before the full board for discussion due to safety concerns (i.e., Site Addition to Protocol xForms, Miscellaneous Submission xForms, etc.), will not require completed all member checklists, but must still be reviewed by each attending member.

Primary and secondary reviewers may notify the IRB staff via email prior to a meeting (or verbally as need becomes apparent during the meeting) to request the use of a consultant. The reviewer will need to state the purpose of the consultant, what expertise the consultant shall have, and recommend a consultant if they are able to do so (e.g., retinal specialist).

3.1.3. IRB Member Compensation

The JCHR IRB Members that are employed by JCHR do not receive additional compensation for their service on the IRB. These members have an adjustment in percent allocation of workload to account for the activities on behalf of the IRB (e.g., 5% FTE). The JCHR IRB Members that are not employed full time by JCHR are compensated on a quarterly basis for activities as follows:

- Each Completed Expedited Review: $10.00
- Each Full Board Meeting Attended: $200.00
- Each Full Board Meeting Attendance as leading Chair: $250.00

NOTE: Any compensation received by JCHR for non-employed IRB Members is tax reportable and the IRS requires reporting of amounts received in a calendar year $\geq$ $600.00.

3.1.4. IRB Member Attendance

In order for IRB Members to receive their stipend, they must have completely fulfilled their obligations as a member, which includes full participation in any board meetings and completion of verbal and documented reviews. If IRB members do not fulfil their obligations, then they will not receive a stipend for that activity. Concerns regarding performance (e.g., not completing reviews with documentation by specified deadlines) or attendance may be grounds for termination from the IRB. The IRB does not have a set requirement for attendance to allow flexibility for extenuating circumstances (e.g., maternity leave, jury duty). However, the IRB will evaluate repeated absences without extenuating circumstance as possible cause for termination.

Further, the IRB Members will be provided training no less than annually on applicable policies and procedures and will be required to return their attestations or other documentation of training to the JCHR IRB Staff. Members will also need to provide CVs/Biosketches as updated, and complete annual Conflict of Interest Disclosure forms no less than annually (HRPP/IRB Policy Number 2012.04/02). If member materials are not provided by the due date as set forth by the JCHR IRB staff, that member may not be permitted to participate in IRB meetings until the requirements are met.

3.1.5. Duties and Qualifications of the IRB Members

Scientific Members: A member is considered a "scientific member" when he/she has at least a Masters Degree in a scientific or medical field, and has clinical or research-related experience. These members typically have MDs, or have MS degrees with additional research-related certification (CCRP or CCRA). These members are responsible for serving as primary or secondary reviewers of full board applications to ensure that protocols are being reviewed by someone with the scientific knowledge to adequately review such submissions. They may also serve as primary reviewers for expedited reviews of other submissions.

Non-Scientific Members: These members are most commonly referred to as "participant advocates". These members often have a community interest (e.g., social work, community boards) and may have direct interest in the subjects' perspectives (e.g., have been subjects themselves, have children with diabetes). The non-scientific members serve the board primarily by focusing on subject materials (e.g., consent forms, fliers, instructions) to ensure that the interest of the subjects are being served and that the subjects would be able to understand the materials in a language understandable to a non-scientific person. Some non-scientific members that are affiliated with JCHR have site or administrative experience and so may be designated to perform primary reviews of certain expedited submissions (e.g., site applications, site changes to ICFs).

Affiliated Members: Both scientific and non-scientific members may be affiliated with JCHR. A member is considered "affiliated" when they have responsibility under the JCHR in a way other than as an IRB Member. The most common example of an affiliated member would be a member that is employed by JCHR in one capacity, and serves on the JCHR IRB in another.

3.1.6. Additional Duties and Qualifications for Chairs

The JCHR IRB currently only permits physicians to serve as Chairs or Vice Chairs. None of the Chairs or Vice Chairs are affiliated with JCHR. These members have the added responsibilities of facilitating meeting discussion, encouraging differing perspectives, overseeing full board meetings, calling board meeting submissions to votes, and assisting in the evaluation of IRB Members among other things. The Chairs, Vice Chairs and the IRB Administrator are also the only members that can review immediate safety submissions (e.g., SAEs, UPs, Significant Deviations - although all qualifying submissions are brought before the full board for discussion), and approve the IRB Meeting Minutes. The IRB Administrator must be a scientific member, but is affiliated with JCHR as they run the JCHR IRB department under the supervision of the Director of the HRPP.

3.1.7. IRB Member Assessments

All IRB members are assessed on an annual basis and are provided with their assessments for review/comment. These assessments are reviewed with the Director of the HRPP and an IRB Chair. Feedback and comments are strongly encouraged from the IRB Members. After reviewing their assessment, IRB Members must sign, date, and return their assessment form to the IRB office (HRPP/IRB Policy Number 2013.12/10).

3.1.8. IRB Staff Reviews

Per HRPP/IRB Policy Number 2013.12/11, IRB staff members will be assessed on an annual basis except when they are classified as a new hire. New hires are evaluated roughly one and three months after the employment start date. The IRB Administrator performs the evaluation of the IRB staff. The Director of the HRPP performs the evaluation of the IRB Administrator (as applicable). The Chief Operating Officer performs the evaluation of the Director of the HRPP.

3.1.9. Quorum Requirements

If an IRB Committee is unable to maintain quorum during a meeting, voting will cease until quorum is restored. If at least one IRB Member who represents the general perspective of the participants, one IRB Member whose background is scientific, one non-scientific, and one non-affiliated IRB Member is not present during a convened meeting, the quorum is lost and voting cannot be completed until quorum is restored, even if > 50% of that IRB's Committee Members are present. Any member who is recused from voting on an agenda item cannot be counted towards the required quorum and quorum will need to be re-established with eligible members. Members who abstain from voting remain counted for quorum. The quorum majority (>50% and no less than 5 members) is applicable to each committee. For example, there may be 20 total JCHR IRB Members, but 10 on one committee and 10 on another committee, and so majority for quorum for each committee would be 6 members. Further, alternates are not counted towards the total membership of a committee, but will count towards quorum when they are filling in for another member (HRPP/IRB Policy Number 2013.10/04).

3.1.10. Verification of Quorum

In accordance with HRPP/IRB Policy Number 2013.10/05, before the start of each convened meeting, the IRB Administrator (or Chair/Vice-Chair) will verify quorum. Each member will also be asked about any potential conflicts with any applications to be reviewed during the meeting. This is to ensure that quorum will be maintained for all reviews as members with conflicts are not permitted to be present for or vote on reviews for which they have a conflict. It is important to note that if a member is unable to review all materials for a submission or steps out of the room during discussion of a submission, they will be required to abstain from voting on that submission. Abstentions count towards quorum, but not towards the overall decision on a submission. Verification of quorum will be recorded in the IRB meeting minutes along with the corresponding meeting's attendance. Approval of the meeting minutes will be made by an IRB Chair or Vice-Chair in attendance at the applicable meeting, and the IRB Administrator. All IRB members will have access to the meeting minutes.

3.2. IRB Coverage

In accordance with HRPP/IRB Policy Number 2001.08/01, coverage by the JCHR IRB is for JCHR investigators and other sites participating in JCHR-conducted studies. Upon request, and after review by the Executive Director, the JCHR IRB may also consider IRB coverage for other sponsored or investigator-initiated research.

3.2.1. IRB Coverage for Other Sponsored or Investigator-Initiated Research

The JCHR IRB may perform reviews for human subjects research protocols of other sponsored or investigator-initiated research, and for corresponding site submissions under those protocols. The JCHR IRB will conduct all reviews in accordance with 45 CFR 46, 45 CFR 160 and 164, 21 CFR 50, and 21 CFR 56, as well as all other applicable regulations and guidances for the protocol specified herein. The reviews by the JCHR IRB will be performed and charged to the Sponsor as indicated in an executed Service Agreement {LINK} in accordance with the Fee Schedule {LINK} as specified for the corresponding study. The Sponsor will be charged for the site submissions under the protocol as well.

The specified fees will be charged for ***each*** review (e.g., full board submission that was deferred to the next board meeting due to substantial changes would be charged for both full board reviews). Further, when miscellaneous submissions contain Spanish translations, an additional fee applies for the cost of the translation services provided through the JCHR IRB. The separate translation fee schedule must be approved by Sponsor prior to submission to the JCHR IRB for review. The JCHR IRB does not charge sites for reviews and does not charge for the reviews of safety-related event reporting (e.g., SAEs, Unanticipated Problems, Significant Deviations, Emergency Use Notifications, etc.).

When JCHR study teams will not be responsible for executing clinical trial agreements with sites, reliance on the JCHR IRB will need to be documented, even when the site does not have a local IRB. This must be done via the external Sponsor's clinical trial agreement with the site, and a formal stand-alone reliance agreement with JCHR IRB. (HRPP/IRB Policy Number 2012.03/01 – Site Coverage by JCHR IRB).

3.2.2. Single IRB Usage for Multi-Site Research

The JCHR IRB notes the NIH released a policy on the use of a single Institutional Review Board for multi-site research, notice number: NOT-OD-16-094 and starts the process to offer IRB review as a Single IRB for JCHR coordinated studies (HRPP/IRB Policy Number 2016.06/02). As such, a site that is overseen by a local IRB can request IRB coverage by the JCHR IRB under JCHR IRB approved research only after the JCHR IRB and the local IRB have executed a Reliance Agreement. If a site does not have a local IRB, then they can submit to work on JCHR IRB approved research anytime. Further, a transfer of IRB coverage to the JCHR IRB can be requested as well. However, to do this would require (a) terminating the IRB coverage of the first IRB and (b) re-consenting all protocol participants with a JCHR informed consent form. A Reliance Agreement must be executed prior to IRB submission and review.

Per HRPP/IRB Policy Number 2012.03/01, a site that has access to an institutional IRB can request IRB coverage by the JCHR IRB under the following conditions:

- Approval from the Site's local IRB is granted when the Site is part of a legal entity that has its own local IRB (e.g., not applicable to a private practice that has used an IRB as part of a hospital or another entity before, but is not required to use that IRB otherwise).
- A reliance agreement must be executed prior to JCHR IRB submission for the addition of the Site under a study.
- The JCHR IRB will be the IRB of record for a given study.

Even if a study has already started, the Site may transfer IRB coverage to the JCHR IRB with approval of the local IRB. However, to do this, the Site would be required to (a) terminate the local IRB coverage, and (b) re-consent all active subjects with a JCHR IRB approved informed consent form. A reliance agreement must also be executed prior to IRB submission. When JCHR is serving as the sponsor of a study and will be executing a clinical trial agreement with sites, the sites that do not have a local IRB are not required to execute a reliance agreement, and may submit to the JCHR IRB without any additional action, as the clinical trial agreement will confirm reliance on the JCHR IRB.

3.2.2.1. Reliance Agreements

To establish a reliance agreement, the site must first reach out to the JCHR IRB, or put the JCHR IRB in touch with the local IRB. The two IRB's will work together to establish the terms of the reliance agreement. This will include the completion of a local context form whereby the local IRB is able to inform the JCHR IRB of any state or institutional requirements. The local IRB will also be able to provide a redline to the JCHR ICF template to specify what language they require and in what applicable sections. The JCHR IRB seeks to comply with state laws, and will comply with institutional policy where relevant. This means that while the JCHR IRB will take all comments under consideration, the JCHR IRB seeks to consider changes that will improve the quality of knowledge provided to the subjects, and not seek to make changes that do not appear to add value to the consent process or forms. Once the terms and modifications have been agreed to, the agreement shall be signed by representatives of the IRBs, and then sites can apply to various research studies as specified.

3.3. Investigator Qualifications

In accordance with the HRPP/IRB Policy Numbers 2015.03/03, 2013.11/07, 2017.01/06, and 2017.01/09, before adding a new site principal or co-investigator to a research activity, the JCHR IRB shall evaluate the qualifications of the investigators, and may consider the following: number of years in the field, board certification, previous research experience, human subjects protection training, 483's, investigation into the practice of medicine, and gaps in practice. This will include current CV/Biosketches and proof of licensure (as requested) with applicable submissions for review of qualifications and appropriateness to work on each specified study. Further, the IRB may request the site staff delegation log to support their review.

The JCHR IRB is responsible for assuring that principal and co-investigators are appropriately qualified, competent, and that their intellectual capacity supports participation in clinical research. Should the JCHR IRB have any reservation regarding a new investigator, additional

protections (e.g. more frequent review, observation of the consent process/procedure, etc.) may be required and is at the discretion of the JCHR IRB. NOTE: The principal and co-investigators are responsible for the overall conduct of research at their sites and so are responsible for any and all professionals delegated research-related activities on their behalf.

In the event that a principal investigator is on unexpected leave, the JCHR IRB should be notified within three (3) days of discovering this information, so accommodations (within reason) can be considered by the JCHR IRB. Accommodations may include changing the principal investigator, the JCHR IRB signing off on urgent applications, etc. (HRPP/IRB Policy Number 2013.11/06).

3.3.1. Human Subjects Protection Training

Per HRPP/IRB Policy Number 2011.04/02, the JCHR IRB adapts the NIH requirement for the training in the protection of human subjects. As such, all principal investigators and co-investigators ("site investigators") covered by the JCHR IRB must complete an NIH accepted training for Good Clinical Practice (GCP), as well as all other key JCHR staff and IRB Members. Further, additional material regarding the ethical principles by which JCHR requires research to be conducted, is found in the JCHR IRB Investigator Handbook. The material covered in the Handbook contains a section that addresses the role of the HIPAA Privacy Rule in the research environment. All JCHR and non-JCHR sponsor-investigators, as well as JCHR Protocol Managers and Monitors, and site investigators must complete training on the Handbook.

The obtained GCP training certificate must be submitted as an attachment to applications as required for JCHR IRB review, along with the Attestation of the review and agreement to comply with the JCHR IRB Investigator Handbook. The GCP certificate and Handbook Attestation are valid for three years, except where major changes to GCP or the Handbook are made, in which case retraining will be required. The JCHR IRB will not review an application if these training requirements have not been completed. Incomplete applications will be sent back to submitters. The documented training by JCHR staff as specified, will be tracked in the JCHR Document Management app, or by the Director of the HRPP or designee. For more information on the management of this policy, please see the JCHR SOP HRPP 602 – Human Subjects Protection Training.

Additional research-specific HIPAA training is provided to all JCHR staff annually as documented in the JCHR Document Management app. This training is provided through the Research HIPAA Training presentation {LINK}.

3.4. General Application Submissions for IRB Review

All submitters must ensure that all applications and their supporting documents are complete upon submission via Jaeb.my.IRBManager.com. Principal Investigators are also required to sign off on the applications to attest to completion and accuracy. The software is designed such that required fields must be completed to allow the submitter to proceed with any application to reduce the likelihood that fields will be missed in error. Further, an IRB Coordinator will provide a basic review for completeness (e.g., "upload CV" was requested but instead a picture of car was uploaded). If the IRB Coordinator identifies a discrepancy or requires a clarification, then

the IRB Coordinator will send the application back for completion/correction. Once a final, correct application is received, then an IRB Coordinator will assign the review to an IRB Member per the IRB Administrator. Incomplete/incorrect applications will not be assigned to IRB Members for review.

Site applications cannot be received in IRBManager until the JCHR/Sponsor research has been approved. Further, if the JCHR/Sponsor is requesting an amendment, sites cannot submit updates to customized materials to reflect/incorporate the main amendment until after the main amendment is approved. This reduces the rework of the sites, the IRB Coordinators, and the IRB Members. Finally, JCHR/Sponsors cannot close their study until all sites approved under that study have closed (HRPP/IRB Policy Number 2013.12/08).

3.4.1. Exemptions and Secondary Research Activities

Under the HRPP/IRB Policy Number 2010.10/02, the JCHR IRB may consider research activities involving human subjects conducted under the following categories exempt in accordance with 45 CFR 46 exemption categories:

1. Research is exempt if it is conducted in established or commonly accepted educational settings, that specifically involve normal educational practices that are not likely to adversely impact student's opportunity to learn required educational content or the assessment of educators who provide instruction.

2. Research is exempt if it only includes interactions involving educational tests, survey procedures, interview procedures, or observation of public behavior if at least one of the following criteria is met (NOTE: Sections 2(i) and 2(ii) below only may apply to research involving children for educational testing or the observing public behavior when the investigator(s) do not participate in the activities being observed.):
    i. Information recorded cannot readily be linked back to subjects identity directly or through linked identifiers; or
    ii. None of the information, if disclosed outside of the research, would place subjects at risk of harm (e.g., criminally, financially, reputational, etc.); or
    iii. If information obtained can readily be linked back to subjects' identity, then the IRB has conducted a limited IRB review and determined that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

3. Research <u>involving benign behavioral interventions</u> in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
    i. Information recorded cannot readily be linked back to subjects identity directly or through linked identifiers; or
    ii. None of the information, if disclosed outside of the research, would place subjects at risk of harm (e.g., criminally, financially, reputational, etc.); or
    iii. If information obtained can readily be linked back to subjects identity, then the IRB has conducted a limited IRB review (may be expedited) to make the determination

that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

4. Research using information or biospecimens collected for either (a) research studies other than the proposed research, or (b) non-research purposes (both are known as "Secondary Research"), that use identifiable private information or identifiable biospecimens are exempt if at least one of the following criteria are met:

    i. Identifiable private information or identifiable biospecimens are publicly available; or
    ii. Information, which may include information about biospecimens, was originally captured and recorded in an unidentifiable manner and the investigator does not contact or re-identify the subjects; or
    iii. The investigator's use is regulated under HIPAA as "health care operations", "research" or "public health" (see JCHR HRPP/IRB Policy 2017.12/11 for more information); or
    iv. Research is conducted by or on behalf of a Federal Agency using information collected or generated by the government for non-research purposes, and the information is protected by federal privacy standards

5. Research and demonstration projects which are conducted or supported by a Federal department or agency, and which are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

    NOTE: The applicable Federal Agency will need to publish a list of projects covered by this exemption prior to commencing the research in the future.

6. Qualifying taste and food quality evaluation and consumer acceptance studies.

7. Secondary Research not meeting the criterial above using identifiable private information or identifiable biospecimens is considered exempt ***if*** the following are met (NOTE: This provision is not applicable to JCHR's activities):

    i. Broad Consent was obtained for the use of the private information or identifiable biospecimens as required; and
    ii. The IRB has conducted a limited review (may be expedited) and has made the determination that, when appropriate, there are adequate provisions to protect the privacy of subject and to maintain the confidentiality of data; and
    iii. Documented informed consent (see (i) above) for Secondary Research use of the private information or identifiable biospecimen was obtained, or a waiver of consent was granted by the IRB when one of the following applies:

a. An informed consent form would actually become the only link to a subject and that link would have potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
b. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
c. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained

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

iv. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

*NOTE: Research involving interaction or intervention with human subjects to collect information or biospecimens is **not** considered Secondary Research, it is primary research (i.e., requires IRB review). In addition, "Secondary Research" that is **only** using non-identifiable information or biospecimens is **not** human subjects research (i.e., does not fall under the scope of these regulations).*

8. The storage or maintenance of identifiable private information or identifiable biospecimens for future research is considered exempt ***if*** the following are met (NOTE: This provision is not applicable to JCHR's activities):

i. Broad Consent was obtained for the storage and maintenance of the private information or identifiable biospecimens; and
ii. The IRB has conducted a limited review and has made the determination that:
    a. Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements;
    b. Broad consent is appropriately documented or waiver of documentation is appropriate; and
    c. If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

NOTE: Per 45 CFR 46, the exempts above may only be applied to vulnerable populations as described below:

1. Each of the exemptions of this policy may be applied to research involving pregnant women, human fetuses and neonates, ***if*** the conditions of the exemption are met.

NOTE: The regulations of 21 CFR 56 do not permit exemption from IRB review for IND or IDE studies submitted after 1981.

If a JCHR researcher believes that an activity may qualify for exempt categorization, then the researcher must submit a Request for Exempt Categorization application with all supporting documents, to the JCHR IRB for review. In order to grant exemption status, the designated reviewer will utilize the policy described above as the basis for their decision. The IRB Chair, Vice Chair, and the IRB Administrator are the only members that may grant exemption status, but the board will be notified of all exemptions at a full convened board meeting.

3.4.2. Initial Reviews of JCHR/Sponsor Research

In accordance with HRPP/IRB Policy Number 2001.08/02, all initial applications seeking to conduct human subjects research must be submitted through Jaeb.my.IRBManager.com (a web-based system). This application is required for any human subjects research that does not qualify, as confirmed by the IRB, for expedited review, or exempt categorization. In accordance with the regulations, initial reviews will include the determination that all applicable requirements have been satisfied (see HRPP/IRB Policy 2010.10/05 – Approval Criteria for more information).

3.4.3. Continuing Reviews

Per JCHR HRPP/IRB Policy 2001.08/03 Continuing Review, once research has been approved, continuing review applications will be submitted for review at intervals appropriate to the degree of risk, but no less than once a year. Unless, in accordance with the "2018 Requirements", the study meets the certain circumstances when a continuing review of research is not required. In general, a continuing review is not required for research initially approved on or after 21 Jan 2019 that:

1. was approved under an expedited review (i.e., no greater than minimal risk, and meeting one of the Categories of Research Activities eligible for expedited review);
2. was considered exempt and required only a limited IRB review
3. has completed all interventions and only involves the following:
    a. analyzing data (including identifiable data or biospecimens)
    b. accessing follow-up data as part of clinical care

However, any FDA regulated study (i.e., IND or IDE study) is required to have continuing review until study closure, even if the research has completed all interventions. In addition, the IRB may still choose to require a continuing review for the circumstances above, but the determination must be documented. For example, if the IRB has concerns about conflict of interest, noncompliance, or oversight, then the IRB can require a continuing review. In the event that the IRB determines that continuing review is not required, amendments, qualifying adverse

events, unanticipated problems, and deviations must still be reported as required. To ensure that this documentation is established and to ensure that IRBManager extends the approval period for applicable studies, a brief submission will be made no less than once a year so that the IRB can confirm that the study does not need a continuing review, or state why it does.

Both JCHR/Sponsor research and sites must have continuing reviews. In accordance with the regulations, continuing reviews will include the determination that all of the applicable requirements have been satisfied (see HRPP/IRB Policy 2010.10/05 – Approval Criteria for more information) except where the IRB determines that continuing review is not required. The For JCHR/Sponsor continuing reviews, reports will be obtained regarding data about all study adverse events, all study deviations (significant, and non-significant), all study unanticipated problems, and all available DSMB/DSMC reports, as applicable.

JCHR IRB has the authority to observe or have a third party observe the consent process and the research.

3.4.4. Amendments to Previously Approved Research

The HRPP/IRB Policy Number 2001.08/04 states that all changes ("amendments") to previously approved human subjects research be submitted through Jaeb.my.IRBManager.com for review. This application is required for any human subjects research and may qualify for expedited review for minor changes, or require full board review for major changes. (See HRPP/IRB Policy 2010.10/03 for more information regarding what qualifies as minor/major changes). In accordance with the regulations, reviews of amendments will include the determination that all of the applicable requirements have been satisfied. Amendments may be submitted by the JCHR/Sponsor or by the sites. Typically, sites will amend the research-related activities at their sites to incorporate site-specific language into consent forms or add recruitment materials.

For amendments to previously approved research that do not qualify as minor changes under the expedited review process, these amendments will be reviewed by a convened IRB during a board meeting. All members have access to all modified documents. The primary reviewer (and/or secondary reviewer) will be provided with and must complete the appropriate checklists.

3.4.5. Closure of Research Activities

Per the HRPP/IRB Policy Number 2001.08/05, and in accordance with the regulations, research activity closure reviews will include the determination that all of the applicable requirements have been satisfied. All sites with approval to conduct research under a given protocol must close research activities with the applicable IRB prior to the JCHR/Sponsor submitting for closure. The closure submissions to the IRB will include information regarding the reason for early closure, as applicable, any events that have not yet been reported, and any publication/manuscript materials available.

3.4.6. Adverse Events

Per the JCHR HRPP/IRB policy 2001.08/06, certain qualifying adverse events must be reported immediately. The definitions used are from the JCHR SOP CT: 202 – Adverse Event and Device

Reporting as interpreted from the federal regulations and guidance documents of Good Clinical Practice. Site Investigators are required to report all ***serious***, adverse events ***related*** to the study in any human subjects research activity, regardless if the event was expected/anticipated, to the JCHR IRB promptly (**within seven (7) calendar days**) when the JCHR IRB is the overseeing IRB of the site where the event occurred. This report will be made using the Adverse Event/Unanticipated Problem Reporting xForm via Jaeb.my.IRBManager.com.

Further, if the sponsor (JCHR or Non-JCHR) believes that the event in an IND study qualifies as ***serious, related to the investigation product (including control/placebo in blind studies), unexpected*** adverse event (SUSAR), then the sponsor must report this to the FDA and all participating investigators within fifteen (15) calendar days after making the qualification determination. For a SUSAR that is ***fatal or life-threatening***, the sponsor (JCHR or external) must notify the FDA (and investigators) as soon as possible but **no later than seven (7) calendar days** after JCHR initial receipt of the information. The JCHR IRB will still be notified within seven (7) calendar days of the identification of any SUSAR.

For IDE studies, the sponsor (JCHR or Non-JCHR) must report any ***serious, related (to the study), unanticipated*** device effects (UADEs) to the FDA, ***all reviewing IRBs***, and participating investigators **within 10 working days** after receiving the notice of the effect. The JCHR IRB still requires notification within seven (7) calendar days of the identification of any UADE.

Also, if the sponsor determines that an UADE presents an ***unreasonable risk*** to subjects, then the sponsor will terminate all investigations or parts of investigations presenting that risk as soon as possible. Such termination shall occur no later than **5 working days** after the sponsor makes this determination and no later than **15 working days** after the sponsor first received notice of the UADE. If the device is a significant risk device, JCHR cannot resume a terminated investigation without IRB and FDA approval. If the device is not a significant risk device, a sponsor may not resume a terminated investigation without IRB approval.

That means that for a JCHR IRB covered site, the IRB shall receive one notice from the site investigator that states an event was serious and related, and then if the sponsor determines the event is a SUSAR or UADE, another report will be made to the IRB from the sponsor about the same event later.

NOTE: Adverse events that are not serious and related to the study need only be submitted as a log in the continuing review submission by the sponsor. This log will contain all adverse events for all study sites, even if they are not overseen directly by the JCHR IRB. This enables the JCHR IRB to evaluate trends. The sponsor may specify which sites are JCHR IRB sites in their report/log. For other unanticipated problems that do not meet the definition of an adverse event, please see JCHR HRPP/IRB policy 2014.09/06 – Unanticipated Problems. Such problems may include device malfunctions, pregnancy, and consent issues, and may still require immediate reporting under this category.

3.4.7. Unanticipated Problems

Per the unanticipated problem policy (HRPP IRB Policy Number 2014.09/06), the JCHR IRB considers *unanticipated problems*, in general, to include any incident, experience, or outcome that meets ***all*** of the following criteria:

1. ***unexpected*** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol related documents, such as the IRB approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;

2. ***related or possibly related*** to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

3. suggests that the research places subjects or others at a ***greater risk*** of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Site Investigators are responsible for reporting all unexpected instances that are possibly related to participation in the research promptly (***within seven (7) calendar days*** of recognition). These unexpected instances should be submitted to the IRB through Jaeb.my.IRBManager.com by completing an Adverse Event/Unanticipated Problem Reporting xForm. Sites are instructed to submit serious adverse events related to the study (not just the intervention) as it helps make the determination regarding unanticipated problems.

JCHR/Sponsors must also report all unexpected instances not directly involving a specific site that are possibly related to participation in the research promptly (***within seven (7) calendar days*** of recognition). An example of this type of event would be that the devices are malfunctioning across the study and this trend did not lead to a specific event at a site, but could impact subject safety if not corrected.

An unanticipated problem may or may not be an Adverse Event (AE). If the event is a qualifying AE, then additional reporting may be required. Once an investigator has identified that an event meets the unanticipated problem criteria and reports the event as such, the IRB will review for verification and assess the actions taken to mitigate any risk presented from the event, which may include whether the risk assessment for the study should be changed. If the IRB determines that the event is in fact an unanticipated problem, the IRB must report the event to the Director of the HRPP immediately so that the Director can report the event to OHRP accordingly. Additional reporting by the JCHR IRB to the local institution may be required under terms of the Reliance Agreement as well.

3.4.8. Deviations and Noncompliance

In accordance with HRPP/IRB Policy Number 2001.08/07, and since the investigators may not have a clear understanding of what constitutes serious or continuous noncompliance, the IRB requires that the investigator report any significant deviation to the IRB for the IRB's determination of noncompliance. For more information regarding this process, please review the JCHR SOP HRPP 604: Noncompliance.

***Significant Deviation*:** Any deviation that departs from the established materials in such a way that it poses an increase in the risk to participants, adversely affects the welfare, rights, and safety of the research participants, or negatively influences the scientific study integrity.

The JCHR IRB requires immediate reporting (***within seven (7) calendar days***) of all significant deviations. Some examples that impact risk include deviations to informed consent, eligibility criteria, potential HIPAA violations, and investigational product usage, but this is not a comprehensive list. When such a deviation is being examined to determine if it is significant or not, think about the definition and ask "Does this deviation pose an increased risk to participant's rights, safety or wellbeing, or pose a risk to the integrity of the study or data?"

Significant deviations and/or noncompliance will be submitted to Jaeb.my.IRBManager.com using the Significant Deviation/Noncompliance Reporting xForm. Non-significant deviations may be held and reported during the continuing review submission, which requires a report of all deviations (both significant and non-significant). The JCHR IRB will be responsible for determining if a significant deviation and/or noncompliance meets the criteria for serious or continuous noncompliance. If the criteria is met, then the IRB must notify the Director of the Human Research Protection Program (HRPP) immediately as the Director will be required to report such instances to the OHRP and FDA, as applicable. Additional reporting by the JCHR IRB to the local institution may be required under terms of the Reliance Agreement as well.

3.4.9. Emergency Use

Per the JCHR HRPP/IRB Policy 2017.12/13, the JCHR IRB does not plan to provide coverage for emergency use of investigational product. In the event however that a JCHR IRB covered investigator has used investigational product without adequate informed consent solely to sustain the life of a subject, then the investigator must report this use (see the written certification below) to the JCHR IRB and the FDA ***within five (5) working days*** in accordance with the FDA regulations. This notification will be made using the Emergency Use Notification xForm via Jaeb.my.IRBManager.com. The IRB is then responsible for evaluating the use and ensuring that it did in fact meet the acceptable criteria for use.

Before an investigator can use the investigational product for emergency use, the investigator ***and*** a physician who is not involved with the investigation, must certify ***in writing*** to all of the following:

1. The human subject is confronted by a life-threatening situation necessitating the use of the test article;
2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject;
3. Time is not sufficient to obtain consent from the subject's legal representative; and
4. There is no alternative method available of an approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

3.4.10. Subject Materials

IRB approval is required for written or printed materials (e.g., recruitment flyers, questionnaires, brochures, letters, non-commercial user guides, etc.) that will be provided to or seen by study participants regarding the study or study results. In addition, IRB approval is required for presentation of study results on a public website as reviewed in the informed consent forms. Further, once scripts for materials are produced, such as radio ads or instructional videos, the produced recording must be submitted for IRB acknowledgement prior to running. Additional requests for changes once the decision letter has been sent will not be considered without another submission, unless it is to correct an IRB error (e.g., footer changed in error, decision letter worded incorrectly). Please see HRPP/IRB Policy Number 2014.07/05.

3.4.11. Scientific Engagement Only

The JCHR researchers may submit applications for scientific engagement only activities. These applications are to capture reviews as

(1) Required by a funder (e.g., foundation) to obtain a grant, but where that grant would be used to support various protocols that will be submitted separately for specific IRB review of human subjects research under each protocol, or
(2) Where the research itself is being overseen by another IRB and the JCHR researcher is following the JCHR process of receiving IRB review of JCHR's activities as a contractor under that research.

Because of the nature of the scientific engagement only review, these applications will be reviewed as expedited by an affiliated IRB Member, although all reviews will be shared with the full convened board.

3.4.12. Miscellaneous Submissions

The JCHR IRB will review miscellaneous submissions of activities that do not fall under the scope of other submissions. The submissions may include a certified translation of previously approved English material into Spanish, notifications, or other information. If the miscellaneous submission was used, but the IRB Staff believe that another application would be more appropriate, then the IRB Staff have the authority to return the submission to the specified party and require another application be submitted. This is to ensure that the relevant information is obtained on the application to provide the IRB Member with the necessary information to complete their review and make a determination.

3.5. Methods of Review

3.5.1. IRB Full Board Meetings

In accordance with HRPP/IRB Policy Number 2010.10/04, all human subjects research activities that do not meet the requirements for exempt status or expedited review will be submitted and reviewed by a convened IRB Committee ("full board meeting"). The meetings will typically be held at JCHR in person, however, there may be circumstances where the meetings are held through remote conferencing (e.g., weather does not permit physical attendance). Decisions regarding full board reviews made by a convened IRB Committee are: (a) acknowledged, (b) approved, (c) approved with specific modifications, (d) defer, (e) not approved, (f) suspended, and (g) terminated.

The JCHR IRB meets no less than once per month to review initial application requests, amendments, and renewals of research projects. The schedule of IRB meetings, submission deadlines and applications are available on the JCHR Intranet. Full committee review requires more preparation time for both the investigator and the committee than expedited reviews or exempted research. Any controverted issues discussed during the IRB meeting or lack thereof will be included within the meeting minutes. At the beginning of each IRB convened meeting, the IRB Administrator discusses business items and includes a detailed description of any exempt reviews and safety event reviews needing full board reporting, performed since the last IRB meeting.

All checklists must be completed prior to the start of the meeting. The primary reviewer (or secondary reviewer in the event of the primary reviewer's absence) will provide an overview of what was submitted, identify any questions or concerns, and then will make a recommendation. The secondary reviewer (unless the primary review was absent) will share where there is disagreement with the primary reviewer, provide additional information, as applicable, identify questions or concerns, and then will make a recommendation. All other members will then provide any additional thoughts, questions, or concerns based on their reviews. This is especially important for subject materials as they were interpreted by the non-scientific members. Once the discussion is complete, the Chair leading the meeting will call the submission to a vote. The members will then vote and the outcomes will be documented in the meeting minutes.

3.5.2. Expedited Reviews

This process is a review of proposed research by the JCHR IRB chair(s) or an experienced reviewer (as designated by the IRB Chair(s), assigned by the IRB staff, under the supervision of the IRB Administrator), rather than by the full committee. Federal rules permit Expedited Review for certain kinds of research involving no more than minimal risk and for minor changes in approved research. In accordance with the JCHR HRPP/IRB policy 2010.10/03, an expedited review process may be followed for certain activities.

To be eligible for approval via the expedited review process, a research activity must always meet the following conditions:

- The activity must present no more than minimal risk to human participants; ***and***
  - It must be an activity listed in one or more of the Categories of Research Activities Eligible for Expedited Review, as listed below (Section A); ***or***
  - It must be an activity for which only minor changes to previously approved research activities are being requested as listed below (Section B)

A. The JCHR IRB may use the expedited review procedure to review any of the following: For some or all of the research listed in the Notice of the Federal Register (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html) unless the reviewer determines that the study involves greater than minimal risk:

1. Clinical studies of drugs or devices that do not fall under the IND or IDE regulations (see the Notice of the Federal Register above for additional details)

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture (in reasonable quantities and frequencies based on the population - see the Notice of the Federal Register above for additional details)

3. Prospective collection of biological specimens for research purposes by noninvasive means, e.g., hair or nail clippings (see the Notice of the Federal Register above for additional details)

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications)

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis), except when classified as exempt

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

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

8. Continuing review of research previously approved as expedited by the IRB, given that it does not now present greater than minimal risk (full board) or qualify as exempt per HRPP/IRB Policy 2001.8/03, and is not an FDA-regulated study

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

NOTE: This list applies regardless of the age of subjects, except as noted: The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the

subjects: financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The standard requirements for informed consent (or its waiver or alteration) apply regardless of the type of review utilized by the JCHR IRB.

B. For minor changes in previously approved research during the period in which approval is authorized. As such, minor changes such as the addition of site-specific requirements that do not change the level of risks, the research design or methodology, or the subject population may be appropriate for expedited review (e.g., adding a state-required Bill of Rights, Translation of an IRB approved ICF into Spanish, etc.). Therefore, expedited review may be appropriate for the addition of recruitment or other subject material that is consistent with the previously approved research materials (i.e., protocol and informed consent forms). Also, applications submitted to add new sites or new investigators to research activities that have been approved by the JCHR IRB may be reviewed under expedited review as a minor change to previously approved research activities. In the event that the expedited reviewer determines that the site or investigator present a greater than minimal risk (e.g., lack of experience, nature of practice different from typical for this research activity, etc.), the reviewer can defer to the full board for review during a convened meeting. Further, specific changes required by the full board may be approved without going back to a fully convened board in accordance with the JCHR HRPP/IRB policy 2017.12/10 IRB Requests for Modifications.

3.6. Approval Criteria of Human Subjects Research

In accordance with the HHS and FDA requirements, the JCHR IRB follows JCHR HRPP/IRB policy 2010.10/05 regarding the criteria that must be met to approve research. (NOTE: JCHR will not be participating in regulatory Broad Consent). In accordance with the policy, certain criteria apply to both initial review and continuing review of research and provide the framework for the IRB's evaluation of human subjects research. In order to approve, or continue approval, for human subjects research activities, the IRB must determine that all of the following requirements are satisfied:

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

3. Selection of subjects is equitable (IRB shall take into account the purpose, setting and populations of research);

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative in accordance with, and to the extent required by, HHS and FDA regulations;

5. Informed consent will be appropriately documented or waived in accordance with, and to the extent required by, HHS and FDA regulations;

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects; ***and***

7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

NOTE: When the research activities involve some or all subjects that are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, fetuses, prisoners, individuals with impaired decision-making capacity or economically or educationally disadvantaged persons, then additional safeguards have to be included in the study to protect the rights and welfare of these subjects.

3.6.1. Approval Periods

In accordance with HRPP/IRB Policy Number 2014.02/01, research will typically be approved for one year. The studies and corresponding materials are effective through the date prior to the expiration date provided (e.g., if the expiration date is June 2nd 2018, then the approval is valid until 11:59pm on June 1st, 2018). Under policy 2001.08/03 Continuing Review, which allows the waiver of a continuing review, the studies will still be approved for extension no less than annually.

Also, in accordance with the risks to the participants, the JCHR IRB has the authority to require reviews more frequently than once a year. For instance, the JCHR IRB may approve a protocol for 6 months. The shorter approval period will be expected for JCHR/Sponsor studies that meet one or more of the following criteria:

- Phase I clinical trials
- Phase II clinical trials with minors
- Phase III clinical trials with no prospect of direct benefit for minors
- Other high risk protocols as identified by the IRB

Site level applications may remain on an annual review cycle even if they are under a clinical trial that has a review cycle that is more frequent. The web-based system, IRBManager, automatically sets and tracks approvals and expirations in the system. This includes notifications and alerts of upcoming expirations. In the event a site or JCHR/Sponsor has a lapse in coverage, they will be notified by the IRB and informed that their activities are administratively suspended

until the issue is reconciled. They will be given thirty (30) days to submit a continuing review and must include an explanation for the delay as well as confirmation that no activities were conducted during the lapse. If the response is inadequate or if one is not provided, then the IRB may take suspension or termination actions as described in the applicable policy.

3.6.2. IRB Requests for Modifications of Research Activities

Per the HRPP/IRB Policy 2017.12/10, the IRB (or IRB Expedited Reviewer) may require that changes or clarifications be made to protocols and corresponding material in order to approve a particular submission. This policy outlines the process for how these changes or clarifications are to be handled. Wherever possible, the IRB will seek to make specific requests to improve understanding of expectations.

When the IRB requests that specific changes be made (e.g., sending a redline/tracked informed consent form with exact changes being requested), or an expedited reviewer requests changes to an expedited submission, then the Board or reviewer may "approve with changes." In these cases, IRB Administration will send the submitter and Principal Investigator an email summarizing the changes requested, attach any redline/tracked documents, as applicable, and may make specific notes within the application (xForm) for clarity. Once the submitter and/or investigator have made the appropriate changes (including uploading new versions of a document, as applicable), the application can be re-submitted for review. The changes will be sent back to the primary reviewer only (unless, for specific changes requested by the full board, the primary reviewer was/is unavailable (i.e., emergency), in which case the secondary review will be sent the changes). If a submission was "approved with changes" at a full board meeting but the submitter and/or investigator do not accept the proposed specific changes made by the Board or reviewer, and/or they may make additional proposals, the submission will be sent back to the IRB for full review at the next available convened meeting.

When the IRB requests non-specific changes or clarification (e.g., did you mean A or B, what is your process for … and how will you report it) the submitter and investigator will be notified that the application has been deferred. These changes will need to be addressed in the application (xForm). Once the changes or clarifications are made and submitted, the IRB Office will review the application (xForm) to make sure all items were properly addressed, and then the updates will be provided to the IRB at the next available convened meeting for review. At this time, the IRB may vote to approve as clarified/changed, request additional changes, or disapprove the revised submission. If additional changes or clarifications are requested, the process will begin again as stated above, whereby specific changes for acceptance can be made without going back to the IRB at a convened meeting, or whereby non-specific changes or clarifications will need to go back to the IRB at a convened meeting.

3.6.3. Suspension and/or Termination of Research

Per HRPP/IRB Policy Number 2013.01/02, if a site or a JCHR/Sponsor study is seriously and/or repeatedly noncompliant with the IRB's requirements or investigational plan in such a way that it presents unexpected serious harm to subjects, then the IRB may suspend or terminate the approval under the research. A suspension shall be implemented when the IRB will allow the site or the JCHR/Sponsor to implement specific corrective actions to the satisfaction of the IRB in

order to remove the suspension. A termination shall be implemented when the IRB has determined that after corrective actions have been implemented, or in cases of willful intent, the site or JCHR/Sponsor are no longer demonstrating appropriate conduct and shall no longer be permitted to conduct the research. The IRB will notify the Director of the HRPP, and the Director will be required to report the suspension or termination of research activities to the OHRP, FDA or other funding agencies (as applicable). Further, in accordance with the Reliance Agreements established with local IRBs, the JCHR IRB may also need to report to the local IRB.

In the event that a site or JCHR/Sponsor study will be suspended or terminated, the documentation of this action will be tracked with a submission in IRBManager. The documentation shall include the management of any and all active participants. For example, will the active participants be transferred to another site, will the active participants be permitted to continue but new recruitment suspended, will active participants need to have final visits in preparation for final termination, etc. The determination will state the reason for suspension or termination and will identify any issues that have resulted in the suspension or termination.

3.7. IRB Review of Data and Safety Monitoring

Data safety and monitoring is the responsibility of the sponsor and is commonly assigned to an additional review by a Data Safety and Monitoring Committee or Board (DSMC/DSMB). Per JCHR requirements, prior to the initiation of recruitment for a protocol, the DSMC/DSMB must approve the study protocol and study related documents. Subsequent protocol changes that are substantive must also be approved by the DSMC/DSMB prior to implementation. Further, before a protocol is submitted to the IRB, JCHR requires a senior statistician to review the protocol and take responsibility for the statistical analysis plans. None of the DSMB/DSMC members or statisticians serve as members of the JCHR IRB.

Typically, each DSMC/DSMB provides periodic monitoring of research activities according to the plan approved and discussed by the committee. The DSMC/DSMB reviews the ethical conduct of the study and monitors the data for evidence of adverse or beneficial treatment effects. Although each DSMC/DSMB is different, they periodically review the progress of each protocol involving participant safety (at least twice each year).

The DSMC/DSMB is advisory to the JCHR study teams. In general, JCHR researchers work with the DSMC/DSMB to ensure the DSMC/DSMB plan provides adequate protection for the participants. Further details of the role of the DSMC/DSMB appear in the DSMC/DSMB materials on a project specific basis, if applicable. The reviews of the DSMC/DSMB are provided to the IRB as they are conducted so that, in addition to reports the IRB obtains regarding events from the sites and JCHR/Sponsor (adverse events, unanticipated problems, and deviations), the additional recommendations regarding safety and data can be taken into consideration by the IRB.

3.8. Ensuring Equitable Selection of Research Participants

In accordance with the requirements for the criteria for approving research, the JCHR IRB must review how subjects are selected to ensure that the selection is fair and equitable. The IRB will take into account the purposes of the research, as well as the setting in which the research will be

conducted (as required in 45 CFR 46). The regulations are clear that the IRB "should be particularly cognizant of the special problems of research that involves a category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons." One of the ways that the IRB will ensure equitable selection is by reviewing the recruitment plan as described in the initial research applications, and by reviewing recruitment materials, as applicable. For these reasons, the investigators will need to describe their methods in their initial applications, and must submit recruitment materials (as well as any requests for certain qualifying preparatory to research activities) to the JCHR IRB before they can be used.

3.9. Protection of Participant Privacy Interests

Federal regulations require that research involving human subjects include adequate provisions to protect the privacy interests of participants and to maintain the confidentiality of data. In order to approve a research activity, the IRB shall determine if there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data for subjects in the United States. The Research Compliance Committee (RCC) shall be responsible for ensuring compliance with privacy and data protections for subjects outside of the United States, with the guidance of the Data Protection Officer. Specifically, when data is collected regarding European Economic Area or Brazilian citizens, certain authorization for the collection and processing of Personal Data may be required, in accordance with the General Data Protection Regulation (GDPR/LGPD).

It is important to note the distinction between "privacy" and "confidentiality" in human subjects research as it pertains to US citizens. In general, **privacy** concerns are about the *people* involved in the research, whereas **confidentiality** issues are those associated with the *data* obtained for research purposes.

- **Privacy:** The state of being free from the observation, intrusion, or attention of others.

- **Confidentiality:** In the context of human subjects research, the condition that results when data are maintained in a way that prevents inadvertent or inappropriate disclosure of participants' identifiable information.

Provisions for protecting privacy and/or confidentiality are relevant at all stages of research, including subject identification and recruitment, research participation, and analysis of individually identifiable data. Respect for potential participants' right to privacy requires consideration of their interests in having control over the extent, timing, and circumstances of sharing themselves (physically, behaviorally, or intellectually) with others.

What is considered to be "private" depends on the individual and may vary based on age, gender, ethnicity, socioeconomic class, education level, verbal skills, health, legal status, personality, and the individual's relationship with the investigator. Knowledge of the characteristics of the potential participant population is important in considering research methods that respect privacy. In the context of research, concerns about possible "invasions of privacy" are primarily associated with methods used to obtain information about participants, such as by review of personally identifiable records. When evaluating potential privacy

concerns raised by the use of identifiable private records, the following factors should be considered:

- The original purpose of the records.
- Sensitivity of the information involved (e.g., medical vs. attendance records).
- Potential risk of harm from unintended disclosure of the information.
- Whether the research requires access to the identifiable private information.

In considering the sensitivity of identifiable information, investigators and IRBs should evaluate whether disclosure of the information could be damaging to the participants' reputation, financial standing, employability or insurability, or place participants at risk of criminal or civil liability. Access to and/or use of identifiable information from medical records or clinical databases for research purposes must comply with the requirements of the HIPAA Privacy and Security Rules.

Information collected by observation of individuals can also raise concerns about possible invasions of privacy, particularly when the individuals are unaware that they are being observed and/or the behaviors are observed in "quasi-public" places where individuals have a reasonable expectation of privacy. To minimize potential risks, observations should be recorded whenever possible in a manner that does not allow participants to be identified, either directly or through identifiers linked to them. When identifiers are necessary for the research, adequate provisions for maintaining the confidentiality of the data are required.

JCHR IRB evaluates the provisions to maintain the confidentiality of identifiable data collected as part of the initial submissions. Specific applications include questions requesting the description of the methods used to record the research data to (1) guarantee the confidentiality of the research subjects and (2) define who will have access to the research information. The checklist for these reviews includes a section to examine if the privacy of study participants and the confidentiality of the data will be maintained appropriately. If the reviewer identifies any special privacy and confidentiality issue, then they will need to request clarification or correction.

Further, the Adult/LAR ICF Templates include the HIPAA Authorization. All informed consent forms must include this HIPAA authorization or a site-specific HIPAA authorization that may be provided within the consent form or as an attachment.

3.10. Confidentiality of Identifiable Data

Research involving human subjects must include adequate provisions to maintain the confidentiality of identifiable data. Maintaining confidentiality requires safeguarding the information that an individual has disclosed in a relationship of trust and with the expectation that it will not be disclosed to others without permission, except in ways that are consistent with the original disclosure. Confidentiality in the context of human subjects research also refers to the investigator's agreement with participants, when applicable (i.e., through participants' informed consent), about how their identifiable private information will be handled, managed, and disseminated.

Provisions for maintaining the confidentiality of data are necessary for most research studies. In determining the extent to which confidentiality will be maintained, the nature of the information collected and expectations of potential research participants should be considered. Methods for keeping data confidential range from using routine precautions, such as substituting codes for participant identifiers and storing data in locked cabinets, to more elaborate procedures involving statistical methods, or data encryption. The method(s) selected depends on the nature of the information collected and potential risk to participants from a breach of confidentiality.

Consideration should be given to requirements for data security and retention throughout and following completion of the study. Methods for handling and storing data (including the use of personal computers and portable storage devices) must comply with Institutional policies. Restricted data, including protected health information, must be encrypted if stored or used on portable devices, if removed from a secure location, or if electronically transmitted. Individuals are to be informed about the extent to which confidentiality of their data will be maintained during all phases of the study, including who will have access to the data, what security measures will be used, and where data will be stored. Extensive security procedures may be needed in some studies, either to give individuals the confidence they need to participate and answer questions honestly, or to enable researchers to offer strong assurances of confidentiality. Complete confidentiality should not be promised, however, unless personal identifiers have not been obtained or recorded.

Keeping the identities of participants confidential may be as important (or more important) than keeping the data obtained from/about them confidential, especially in studies where individuals are selected because of a sensitive, stigmatizing, or illegal characteristic. Additional measures to safeguard confidentiality may be considered in these cases, such as with a waiver of or alteration to documentation of consent (see Section 3.13 below).

JCHR IRB evaluates the provisions to maintain the confidentiality of identifiable data collected as part of the initial submissions. Specific applications include questions requesting the description of the methods used to record the research data to (1) guarantee the confidentiality of the research subjects and (2) define who will have access to the research information. The checklist for these reviews includes a section to examine if the privacy of study participants and the confidentiality of the data will be maintained appropriately. If the reviewer identifies any special privacy and confidentiality issue, then they will request clarification or correction. Further, the Adult/LAR ICF Templates include the HIPAA Authorization.

3.11. Managing HIPAA Violations

Potential Health Insurance Portability and Accountability Act (HIPAA) violations that are reported via the Significant Deviation/Noncompliance Reporting xForm shall be reviewed by the Director of the HRPP, and all qualifying events will be reported to the site's local IRB, as applicable. The local IRB/institution will then be responsible for following their policies and procedures to investigate, and shall report to all applicable agencies as the covered entity. The local IRB/institution shall be notified no later than seven (7) calendar days from the expedited and/or full board review. Potential data breaches as they relate to GDPR/LGPD will be evaluated by way of the Research Compliance Committee, as described in the General Data Protection Regulation Operations SOP.

3.12. The Consent Process and Documentation

To support the fulfilment of the requirements as stated in the federal regulations under HHS and FDA, JCHR has established a policy (HRPP/IRB 2014.02/02) to describe when and how informed consent must be documented. In accordance with this policy, the instances and methods used to provide this documentation in accordance with the regulations are described below:

1. Informed consent must be documented by the use of a written informed consent form, approved by the JCHR IRB, and signed by the subject or the subject's legally authorized representative (LAR); ***and***

2. A written copy must be given to the subject or the subject's LAR as signed (a signed copy is not required where eConsent is utilized for a study that is not greater than minimal risk); ***and***

3. The informed consent form must:
    a. Meet all of the requirements of an informed consent form (as shown in the JCHR IRB informed consent templates), and the subject or LAR have had adequate opportunity to read the form before it is signed; ***or***
    b. Be replaced with a written short form stating the elements of the informed consent that has been presented to the subject or LAR, and a summary of the key information that was presented to the subject or LAR as a script (both as approved by the JCHR IRB before use). There must be a witness to this presentation of information. While the subject or LAR is only required to sign the short form, the witness and the investigator must sign both the short form and the summary script. If the short form and script are being used because the subject or LAR are illiterate or blind, the subject or LAR simply need to "make their mark" on the appropriate signature line, and only in this instance may the investigator date their mark as verified by the witness. Copies of both the short form and the summary script must be provided to the subject or LAR; ***or***

4. Except for research activities falling under FDA regulations (e.g., IND or IDE studies), the IRB may waive the requirement for the documentation of informed consent ***if***:
    a. The only record linking the subject to the research activity would be the informed consent form, and the principal risk to the subject would be in the potential breach of confidentiality. Each subject or LAR will have to be asked if they want the link to the research, and their wishes will govern; ***or***
    b. The research presents no more than minimal risk of harm to subject and involve no procedures for which consent is normally required outside of the research context; ***or***
    c. The subject or LAR are of a distinct cultural group or community group in which signing forms is not the norm, the research presents no more than minimal risk of harm, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

NOTE: In cases where the documentation is waived, the IRB may require the investigator to provide the subject or LAR with a written statement regarding the research. Also, regarding the fulfilment of the informed consent requirement that the form be understandable to the subject or LAR, and that the subject or LAR have sufficient time to read the form, the JCHR IRB will allow the consent forms to be translated into Spanish by a certified translator providing a certificate of translation. All of the additional requirements of the informed consent process and documentation must be upheld, meaning that all conversation surrounding the consent process must occur in the subject's or LAR's native language. Further, the entirety of the research related communication must also be in their native language.

3.12.1. Legally Authorized Representatives

In accordance with local law, when an adult lacks the capacity to consent, a ***legally authorized representative*** (LAR) and only a LAR can consent on behalf of the participant to allow that individual to participate in research. The precedence order of LAR status is:

- Attorney in Fact (court documentation required)
- Judicially appointed guardian (court documentation required)
- Proxy:
    - Subject's spouse
    - An adult child of the subject
    - A parent of the adult subject
    - An adult sibling of the subject
    - An adult relative of the subject
    - A close friend of the subject

NOTE: This list is not in order of convenience. If the subject has a spouse with decisional capacity, the adult child cannot consent in the spouse's place. If a proxy provides consent for an adult subject, you must document in the medical or research records how validity of the proxy was determined (http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0700-0799/0765/Sections/0765.401.html). The JCHR IRB will only permit (1) attorney in fact (court documentation required), (2) judicially appointed guardian (court documentation required), or (3) one of the following Proxy: subject's spouse, adult child of the subject, or parent of the adult subject to serve as the LAR of an adult who lacks capacity to consent. This will be incorporated into the informed consent form.

Further, Florida considers minors to be anyone under the age of 18 unless otherwise specified. For JCHR, when a minor's participation is being sought for research, the following people may provide consent as a LAR:

- Natural or Adoptive Parents (this does not include step-parents that have not legally adopted the minor)
- Legal Custodians or Legal Guardians
- Emancipated Minor (if self)

These definitions will be included in the Adult/LAR informed consent forms and assent form templates.

3.13. Consent Form Signatures

In accordance with HRPP/IRB Policy Number 2018.08/02, the JCHR IRB requires that consent forms be signed as required by federal regulation and as specified by the IRB.

Consent forms for minimal risk research may be obtained electronically. When they are obtained electronically, as in the case of survey research, the following conditions apply (1) the subject or one LAR, as applicable, may sign the consent form as specified in a digital format, and (2) no researcher or associated staff need sign the consent form.

When research is minimal risk, for consent forms that are completed to document the consent process as it was conducted in person, the following conditions apply (1) the subject or one LAR, as applicable, may sign the consent form, and (2) an Investigator or Investigator's designee on the research staff may sign the consent form to attest to the process.

When the research is greater than minimal risk with a prospect of direct benefit, then the following conditions apply (1) the subject or one LAR may sign the consent form, and (2) an investigator must sign the consent form as part of the consent process.

When the research is greater than minimal risk with no prospect of direct benefit, then the following conditions apply (1) if more than one LAR, as applicable, then both must sign the consent form, and (2) an investigator must sign the consent form as part of the consent process. NOTE: The IRB reserves the right to require more than one LAR sign any consent form and/or require an investigator sign any consent form where the IRB determines that the additional requirements improve subject protections.

3.14. Requests for Waivers/Alterations of the Consent or HIPAA Requirements

In accordance with the JCHR HRPP/IRB Policy 2017.12/11 Requests for Waiver/Alteration of Consent/HIPAA, there are limited circumstances in which a waiver or alteration may be granted to the consent process or HIPAA requirements. Any request for a waiver or alteration of consent and/or HIPAA provisions may be sent to Jaeb.my.IRBManager.com by completing the designated field in the applications. These activities may be reviewed using the expedited review procedure, as applicable.

In accordance with 45 CFR 46 and 45 CFR 164, the IRB may approve a ***waiver*** of the requirement to obtain informed consent/HIPAA authorization, or may approve an ***alteration*** of the informed consent omitting some or all elements of informed consent/HIPAA authorization, for research-related activities ***if***:

1. the research activity involves no more than minimal risk;
2. the research activity could not practicably carried out without a waiver;
3. the waiver will not adversely affect the rights and welfare of the subjects; and
4. wherever appropriate, the subjects or LARs will be provided with pertinent information after participation.

In addition to the regulations described above, the HIPAA Privacy Rule requires that certain processes be followed, and provides for scenarios when a ***waiver*** may be evaluated under a

Preparatory to Research application. The HIPAA Privacy Rule requires a covered entity (e.g., the health care provider) to secure a written authorization from an individual or LAR that gives the researcher permission to use or disclose protected health information ("PHI") for the purposes described in the authorization ***before*** utilizing PHI. This authorization is typically included in the body of the informed consent form, or as a separate form commonly called a "HIPAA Form." An investigator may request a ***waiver*** or ***alteration*** to this requirement by submitting the Preparatory to Research activities through Web IRB. This type of waiver is commonly referred to as a "***partial HIPAA waiver***."

In order for an activity to be considered for this type of waiver, certain criteria must be met as follows:

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

The submissions for Preparatory to Research activities may be reviewed and granted by a designated IRB member under the expedited review procedure, as applicable. Both types of review will require documentation that the IRB has determined that the waiver or alteration meets the criteria as such. The IRB may require the investigator to provide subjects with a written statement summarizing the research even if the informed consent process has been waived or altered.

3.15. Assent and Turning of Age

If a minor, who is currently enrolled in a JCHR IRB approved protocol, turns seven years of age during the duration of the protocol, the minor will be required to provide assent to a JCHR IRB approved investigator at a JCHR IRB approved site during the next study visit. Only one legally authorized representative will be required to attest to the process in the assent document. In general, this policy will apply to intervention studies during the time that the intervention is being received and to studies that involve procedures being done solely for research purposes. As with any protocol, the investigator may request a waiver or other modification of the assent requirement for IRB consideration (HRPP/IRB Policy Number 2015.02/01).

If a minor, who is currently enrolled in a JCHR IRB approved protocol, turns 18 years of age during the duration of the protocol, he or she must be consented by a JCHR IRB approved investigator at a JCHR IRB approved site during the next study visit. As with any protocol, the investigator may request a waiver or other modification of the consent requirement for IRB consideration (HRPP/IRB Policy Number 2015.02/02).

3.16. Posting Clinical Trial Consent Forms

In accordance with the HHS 2018 Requirements effective 21 Jan 2019, JCHR established a policy regarding the posting of clinical trial consent forms (HRPP/IRB policy 2017.12/12). This policy states that, for each clinical trial conducted or supported by a federal department or agency, one IRB-approved informed consent form that was used to enroll subjects must be posted by the awardee of the funds, on a publicly available federal website (to be determined by the federal agency). The federal agency may permit redaction of informed consent information that must remain confidential (e.g., commercial information). The informed consent form must be posted after the clinical trial has closed, but no later than 60 days after the last study visit by any subject.

3.17. Vulnerable Populations

3.17.1. Determining Risks in Vulnerable Populations

If the IRB regularly reviews research that involves categories of participants vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or have experience working with such participants must be present at the convened meeting for studies that are greater than minimal risk. The IRB may choose to invite a representative of the vulnerable population, or may choose to add an additional board member to represent such a population. The determination will most likely be dependent on the frequency of review requests involving a specific vulnerable population.

Applications to the IRB will include questions regarding these subjects and how their rights will be protected, specifically as they relate to additional safeguards. When research protocols involve children as participants the IRB follows the DDHS (45 CFR 46 Subpart D) and/or FDA regulations (21 CFR 50 Subpart D), including the requirements pertaining to approving an appropriate assent process, obtaining assent of children and permission/consent of parents or guardian.

For research involving pregnant women, the IRB is responsible for making the determinations or equivalent protections for pregnant women in accordance with Subpart B of 45 CFR 46. JCHR does not plan to conduct research with prisoners at this time.

3.17.2. Research with Children

For research that involves no more than minimal risk*:*

- The permission of one parent as LAR is required (or only one person as authorized LAR that is not a parent).

For research that involves more than minimal risk with the prospect of direct benefit to the individual children, *the IRB has determined that:*

- The permission of one parent as LAR is required (or only one person as authorized LAR that is not a parent).

For research that involves more than minimal risk without the prospect of direct benefit to the individual children, *the IRB has determined that:*

- The permission of both parents as LARs is required unless one parent is deceased, unknown, incompetent, or not reasonably available, but only one LAR is required if only

one parent or other authorized person has legal responsibility for the care and custody of the child.

(HRPP/IRB Policy Number 2018.08/02 – Consent Form Signatures)

For applicable protocols, the IRB determines and documents that assent is a requirement of:

- All children.
- Some children.
- None of the children.

When the IRB determines that assent is not a requirement of some children, the IRB determines and documents which children are not required to assent. When the IRB determines that assent is not a requirement for some or all children, the IRB determines and documents one of the following:

- The children are not capable of providing assent based on the age, maturity, or psychological state.
- The capability of the children is so limited that they cannot reasonably be consulted.
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
- Assent can be waived using the criteria for waiver of the consent process.

When the IRB determines that assent is a requirement, the IRB determines whether:

- Assent will be documented.
- If so, the process to document assent.

If the following conditions are met, non-therapeutic clinical trials may be conducted on participants with consent of a legally acceptable representative. The conditions are as follows:

a. The clinical trials objectives cannot be fulfilled by means of a trial with participants who can give consent personally
b. There is a low foreseeable risk for participants
c. There is minimal and low foreseeable negative impact on the participant's well being
d. The clinical trial is not prohibited by law
e. When inclusion of such participants comes into question, the opinion of the IRB is sought immediately. Such non-therapeutic trials should be conducted with participants having the disease or condition for which the investigational product was intended. If for any reason the participant appears to be distressed, they should be withdrawn.

Overall, participants in trials such as these must be closely monitored.

3.17.3. Research with Pregnant Women or Fetuses

In accordance with 45 CFR 46.204, pregnant women or fetuses may be involved in research if all of the following conditions are met:

a. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
b. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
c. Any risk is the least possible for achieving the objectives of the research;
d. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when 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, her consent is obtained in accord with the informed consent provisions of subpart A of this part;
e. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
f. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
g. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
h. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
i. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
j. Individuals engaged in the research will have no part in determining the viability of a neonate.

Studies that are determined by the IRB to be no greater than minimal risk will inherently meet the criteria above, may be reviewed by expedited means so long as the applicable Expedited Review criteria are met, and will only require the informed consent of the pregnant woman (not the father). For studies that present greater than minimal risk, the fully convened board will need to assess the criteria and will need to make the determination regarding the additional consent of the father, as well as additional protections for the mother and the fetus. (HRPP/IRB Policy Number 2020.02/01, HRPP/IRB Policy Number 2020.02/02)

3.17.4. Enrolling Family in Research

Recruiting and enrolling family members of the sponsor, CROs, and site staff (study team) may present concerns regarding coercion or undue influence, thereby increasing vulnerability. For this reason, it is the policy of the JCHR HRPP/IRB that such family members may only participate as follows:

1. In research that is no greater than minimal risk; and for children, the JCHR HRPP/IRB requires a parent/LAR that is not on the study team to provide consent; and

2. In research that is greater than minimal risk, but that presents the prospect of direct benefit to the participant, the JCHR HRPP/IRB requires the discussion of consent and the enrollment to be led by someone on the study team that is not a family member, and for children, the JCHR HRPP/IRB also requires that a parent/LAR that is not on the study team provide consent.

Family enrolling in research involving greater than minimal risk without the prospect of direct benefit will not permitted by the JCHR HRPP/IRB policy (HRPP/IRB Policy Number 2019.01/01).

3.18. Enrolling Employees as Human Subject Participants

Recruiting and enrolling employees of a participating institution may present concerns regarding coercion or undue influence thereby increasing vulnerability. For this reason, unless a participating institution has their own policy that is more stringent, it is the policy of the JCHR HRPP/IRB (HRPP/IRB Policy Number 2020.06/03) that employees of a participating institution may only be enrolled as human subject participants in a study as follows:

1. The employee has no role in the applicable research study and the employee's participation in the study will have no effect on their employment at the institution. For example, a study coordinator would not be allowed to participate in the research being conducted in their department, however, an employee from a different department could be considered for enrollment.

2. If the employee does have a role in the applicable research study, or their department is involved, then that employee cannot participate at their institution, but could still participate in the study by enrolling and conducting all applicable study procedures and follow-up visits at a separate institution participating in the study that is independent from their employer.

3.19. Addressing Subject Concerns, Complaints or Requests

The IRB's contact information is available on all Adult/LAR consent forms as a resource for subjects and their legally authorized representatives, as applicable. Further, the contact information of the IRB Administrator and the Director of the HRPP is posted on the www.jaeb.org public website. This website includes a tab for information about research and participating in research, as well as links to other publicly available information, such as clinicaltrials.gov. Subjects that either call or email the IRB will be referred to the IRB Administrator or Director of the HRPP for immediate assistance. If the information provided is indicative of noncompliance or research misconduct, then the reporting of these instances will be investigated and evaluated as described in their applicable SOPs. All correspondence with subjects, legally authorized representatives, and/or potential subjects will be saved in the IRB shared drive, and escalated to the IRB Board and Director of the HRPP, as applicable, in accordance with policies herein.

In the event of a question or concern about a research-related injury or illness, the subjects and legally authorized representatives will also be given the contact information of the investigator and institution within the Adult/LAR consent forms.

3.20. IRB Documentation

In accordance with HRPP/IRB Policy Number 2018.07/01, the JCHR IRB will be receiving submissions and notifications, performing reviews, corresponding with sponsors and sites, maintaining minutes, and providing review letters through the use of a web-based system called "IRBManager" as of the IRB system conversion dated of 08 October 2018. The 15 October 2018 board meeting was submitted in the previous system "Web IRB" and so documentation from that meeting will be the last documentation in Web IRB. Documentation of IRB submissions, reviews and correspondence prior to the conversion date will be housed in Web IRB and/or the IRB shared drive. Most documentation from the date of the conversion to current will be stored in IRBManager (the exception being some email correspondence and reliance agreements, as applicable).

As of the conversion date, all submissions must be made to the JCHR IRB via the IRBManager web-based system. Also, all IRB Members must complete their assigned reviews and corresponding documentation by the deadline provided (for expedited), or prior to the applicable full board meeting (for full board reviews) via this web-based system.

Any changes to an application that the IRB is requiring from the JCHR/Sponsor or investigators will be made through IRBManager. The system allows the primary reviewer and the IRB staff to add comments and notes directly onto the application and then send it back to the submitter/investigator. The submitter/investigator can then make changes to the application, including adding/correcting attachments, and then they can resubmit. Once the application has been resubmitted, IRB staff will ensure all reviewer concerns have been addressed before sending back to a reviewer. If the application is being returned for expedited review, the primary reviewer will reviewer where possible (secondary reviewer in the primary's absence). If the application is being returned for full board, the same primary and secondary reviewers will be assigned where possible. All changes to applications are tracked in IRBManager with an audit trail. The decisions relating to the reviews, and the stamped approved materials (e.g., consent forms) are provided to the investigators (and other staff as applicable), via an automated email from IRBManager.

3.20.1. Reviewer Checklists

All IRB Members who are assigned to review applications as a primary or secondary reviewer are required to complete the corresponding reviewer checklists to verify and ensure all of the correct information is present and adheres to both federal regulations and policies and JCHR policies. Further, all members are expected to review the application (most appropriate for scientific members) or the consent forms (most appropriate for participant advocates) at a minimum, but all materials are available for review before, during and after meetings for all members via IRBManager. All checklists must be completed by the specified deadline (for expedited), or prior to the board meeting (for full board). Checklists that are consistently not completed by the specified deadline or meeting may be cause for IRB Member dismissal from one or multiple committees (HRPP/IRB Policy Number 2013.12/09).

3.20.2. Documentation of Discussions, Decisions and Correspondence

The JCHR IRB keeps a record of full board meeting minutes in IRBManager. The required elements of the minutes are described in the JCHR IRB Minutes Review Checklist template {LINK} in accordance with HRPP/IRB Policy Number 2018.08/03. The required elements include identifying in the minutes when a controverted issue arose and what resolution manifested. JCHR defines a controverted issue as an issue or topic that has differing opinions expressed from different board members where the members are not able to come to consensus during the course of the discussion, the minutes must summarize the IRB's discussion. Resolutions may include requiring modifications to the research for acceptance by the board, deferring the research for continuing discussion and deliberation, or settling by vote, which may include one or more members voting against the research submission.

In addition, all submissions, reviewer checklists, and all decision letters are included and tracked in IRBManager for exempt determinations, expedited reviews, and full board reviews. Correspondence is tracked in IRBManager too, but there may be additional correspondence, such as emails, that will be saved in the IRB shared drive for future reference. For submissions and reviews prior to the implementation of IRBManager, the full documents are housed either in Web IRB with read-only access or in the IRB shared drive and can be printed for future reference.

3.20.3. Retention of IRB Records

In accordance with 45 CFR 46.115(b) and 21 CFR 56.115(b), the JCHR IRB must maintain all relevant IRB records for at least three (3) years after the completion of the research (i.e., closure). The IRB Staff may not destroy any materials without the written (e.g., email) permission of the Director of the HRPP by research protocol. The following is a list of some of the documents that are included in this retention:

- IRB meeting minutes
- Applications and supporting documents submitted for IRB review
- Notes to file
- Correspondence with sites and JCHR/Sponsors
- Policies and procedures
- Reviewer Checklists
- IRB authorization/reliance agreement
- Investigator Handbooks
- Approved materials
- Decision letters

Records are accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner. In the event of an audit or inspection a User Guide for Auditors is available. This user guide provides instructions on accessing the IRBManager system.