THE JAEB CENTER FOR HEALTH RESEARCH (JCHR) INSTITUTIONAL REVIEW BOARD

INVESTIGATOR HANDBOOK

VERSION 12.0
OCTOBER 8TH, 2018

RECORD OF CHANGES

Version	Author(s)	Approver(s)	Effective Date	Revision Description
1.0	Lesley Zajac	Lesley Zajac	23 Sep 1999	First Version
1.1	Lesley Zajac	Lesley Zajac	05 Nov 1999	Provided additional information regarding expedited reviews; clarified the categories that qualify for expedited reviews; formatting
2.0	Lesley Zajac	Lesley Zajac	24 Apr 2001	Incorporated the requirement of ethics training and disclosure of financial conflicts of interest; included information regarding the termination of research activities;
3.0	Lesley Zajac	Lesley Zajac	18 Sep 2001	Formatting edits; addition of several required elements of the informed consent forms
3.1	Lesley Zajac	Lesley Zajac	29 Aug 2002	Added detail about contents of applications; added detail about the full board review process;
3.2	Lesley Zajac	Lesley Zajac	11 Dec 2002	Added more detail about contents of applications
3.3	Marta Baca	Marta Baca	10 Apr 2003	Incorporated into description of 01/01/2007 version
3.4	Marta Baca	Marta Baca	04 Dec 2003	Incorporated into description of 01/01/2007 version
4.0	Marta Baca	Marta Baca	01 Jan 2007	Major formatting changes; added details of the IRB's responsibilities; updated FCOI requirements; added significant detail of the informed consent contents; added information for non-JCHR Investigators; clarified types of projects covered; added information about seeing information on local requirements for Sites; clarified application process and added appendices for references.
4.1	Marta Baca	Marta Baca	16 Feb 2007	Added details on standards for how to consent participants; updated formatting; updated guidance on unanticipated problems and adverse event reviews
5.0	Marta "Baca" Leinberger	Marta "Baca" Leinberger	08 Jun 2009	Updated contact information; added reporting timelines; added definitions and formatting
6.0	Tiffany Piquet	Tiffany Piquet	01 Jan 2012	Entirely reformatted; entire overhaul of policies and procedures
7.0	Tiffany Piquet	Tiffany Piquet	01 Sep 2014	Formatting; added policies on external entities requesting to use JCHR IRB and the incorporation of the IRB reviewer checklists; updated meeting schedule; added information expanding the details of IRB approval; added a section on reinstatement of an inactive/dropped Investigator; added an informed consent checklist; added information on the short form consent process and the Spanish informed consent process; added an attestation form for this handbook

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8.0	Tiffany Piquet	Jennifer Neal-Jimenez	01 Sep 2015	Formatting; added information regarding meetings and deadlines; updated submissions processes and expedited reviews; updates the new Investigator process, updated application process; updated references to policies;
9.0	Jennifer Neal-Jimenez	Jennifer Neal-Jimenez	01 Feb 2017	Formatting; updated meetings and deadlines; updated new Investigator procedures; added information regarding how surveys are to be handled; updated the document submission process and the new Site approval process; incorporated reliance agreement management; updated attachments
9.1	Jennifer Neal-Jimenez	Jennifer Neal-Jimenez	19 Jun 2017	Minor edits; no major changes to policy or procedures
10.0	Jasmine Conner; Kirra Meserve; Jeannie Perkins	Jeannie Perkins	19 Jan 2018	Clarified name for consistency; formatting; the JCHR and Site Investigator Handbooks were combined to create this handbook for consistency, where only minor differences existed, meaning this combined handbook does not change any processes or procedures; aligned with Final Rule changes including the following areas: Section I.1 – Definitions; Section III.1 – Activities under Exempt Categories; Section III.2 Expedited Reviews; Section III.4 and IV.4 Continuing Reviews; Section IX.2 Elements of Informed Consent; Section IX.5 Documenting Informed Consent; Section IX.8 Posting of the Clinical Trial Consent Form; additional changes made for clarification include: Section I.3 Human Subjects Training Requirements; Section IV.5 Amendments to Research Activities and Study Materials; Section IV.5.1 IRB Requests for Modifications; Section IV.6 Recruitment Materials; Section IV.7 Requesting a Wavier/Alteration of Informed Consent or HIPAA Provisions; Section V.1 Reporting Adverse Events; Section V.2 Deviation Reporting and Noncompliance; Section V.3 Reporting Unanticipated Problems; Section V.4 Emergency Use Notifications; Section VIII Ethical Guidelines, Federal Regulations and Good Clinical Practice; Section IX.4 Legally Authorized Representatives
10.1	Jasmine Conner; Kirra Meserve; Jeannie Perkins	Jeannie Perkins	20 Jan 2018	Updated Survey research application number, it is the same as Direct Care; clarified use of the A8; corrected typos, application form names; and formatting discrepancies
11.0	Jasmine Conner;	Jeannie Perkins	23 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;

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	Kirra Meserve; Jeannie Perkins			2010.10/02 Exempt Research; 2010.10/03 Expedited Research; 2017.12/11 Request for Waiver/Alteration of Consent/HIPAA; 2017.12/12 Posting Clinical Trial Consent Forms; 2010.10/05 Approval Criteria. The names of forms were also clarified.
11.1	Jasmine Conner; Kirra Meserve; Jeannie Perkins	Jeannie Perkins	24 Jan 2018	Corrected typos
12.0	Jasmine Conner; Kirra Meserve; Jeannie Perkins	Jeannie Perkins	08 Oct 2018	Reformatted and restructured the entire document based on several updated policies and procedures as well as a new web-based system.

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SECTION 1: INTRODUCTION TO THE IRB

1.1 Purpose of this Handbook

The purpose of this JCHR Institutional Review Board (IRB) Investigator Handbook is to provide training and to serve as a resource to assist JCHR/Sponsors, and Site Investigators submitting for coverage by the JCHR IRB, with the ethical conduct of human subjects research. This Handbook is intended for JCHR/Sponsors leading research activities, their staff that support that research, and the Sites/Investigators that will be conducting the research. This Handbook is consistent with the requirements of the Food and Drug Administration (FDA) and the department of Health and Human Services (HHS) under 21 CFR 50, 54, 56, 312 and 812; 42 CFR 50 Subpart F, 45 CFR 46, and 45 CFR 160, 162, and 164; the principles of Good Clinical Practice, the Belmont Report, and the Declaration of Helsinki; and the standards of the Association for the Accreditation of Human Research Protection Programs (AAHRPP). The JCHR Human Research Protection Program (HRPP) oversees the JCHR Institutional Review Board (IRB), and is accredited through the AAHRPP.

The individuals that are required to read and sign-off on this Handbook are as follows:

- JCHR HRPP and IRB Staff
- JCHR Principal Investigators, Research Managers, Protocol Managers and Monitors
- Site Principal Investigators and Co-Investigators submitting for JCHR IRB coverage

1.2 IRB and HRPP Contacts

JCHR IRB
15310 Amberly Drive, Suite 350
Tampa, FL 33647
Email: IRB@jaeb.org
Phone: 813-975-8690

- For questions/concerns regarding applications and general processes, please ask to speak to someone on the IRB Staff.
- For questions/concerns regarding policies and determinations, please ask to speak to the IRB Administrator.

JCHR Human Research Protection Program (HRPP)
15310 Amberly Drive, Suite 350
Tampa, FL 33647
Email: HRPP@jaeb.org
Phone: 813-975-8690

- For questions relating to specific human subjects protections, or for concerns regarding the IRB's conduct, please ask to speak to the Director of the HRPP.

1.3 Overview of the IRB

The JCHR Institutional Review Board (IRB) is an administrative body established to protect the rights, safety and welfare of human research subjects recruited to participate in research activities conducted by or with JCHR or its affiliates. The JCHR IRB reports to the JCHR Human Research Protection Program (HRPP), led by the Director of the HRPP who reports directly to

the Chief Operating Officer (COO). The COO reports directly to the JCHR Executive Director. The JCHR IRB is made up of the IRB Administrator, the IRB Coordinators, the External IRB and Reliance Specialist, the IRB Chair and Vice Chairs, and the IRB Members.

The JCHR IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and local laws and institutional policies. The JCHR IRB has assured federal regulatory agencies that it will review and approve all research that meet the federal definitions of human subjects research as described herein.

Determining whether or not an activity meets the federal definition of human subjects research is a process. The JCHR/Sponsor must initially determine if the activity meets the federal definition of research and, if so, determine if the activity includes human subjects. The definitions herein will help JCHR/Sponsors and the Investigators assess whether IRB review is required.

Note: The 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 arises, the JCHR will follow the International Conference on Harmonization Good Clinical Practice (ICH GCP E6) guidelines (including updated versions) along with local laws and regulations. (JCHR HRPP/IRB Policy Number 2014.06/04 – Transnational Research).

1.3.1 Federalwide Assurance (FWA)

The JCHR IRB has a Federalwide Assurance (FWA). An FWA is the assurance currently accepted and approved by the Office of Human Research Protections (OHRP). The FWA is JCHR's commitment to department of Health and Human Services (HHS) that it will comply with the requirements in the HHS Protection of Human Subjects regulations found in 45 CFR 46.

The JCHR FWA number is **FWA00000024** and the current expiration is posted on the OHRP Website. These requirements apply to all research conducted under the auspices of the JCHR, regardless of funding source or support.

Coverage by the JCHR IRB is for JCHR/Sponsors leading JCHR research, for JCHR's involvement in the Scientific Engagement of research-related activities, and for the Sites participating in JCHR research. Research led or conducted by the Sponsor, either by JCHR or another Sponsor, is what is referred to herein as "JCHR/Sponsor" (meaning JCHR or an external Sponsor submitting for lead coverage of research, as applicable). Upon request, and after review by the Executive Director, the JCHR IRB may also consider IRB coverage for other sponsored or investigator-initiated research.

1.3.2 Registration with the Office of Human Research Protections (OHRP)

The OHRP provides leadership in the protection of the rights, safety, and welfare of subjects involved in research conducted or supported by HHS. The OHRP helps ensure this by providing clarification and guidance, developing educational programs and materials, maintaining regulatory oversight, and providing advice on ethical and regulatory issues in biomedical and social-behavioral research. The JCHR IRB has been registered with the OHRP under the number **IRB00000766** since December 20, 2000 and the registration expiration can be found on the OHRP Website.

1.4 IRB Membership

An IRB may be made up of one or more Committees. Federal regulations require that membership of each IRB Committee include at a minimum, five members, with varying background and diversity among members. This includes one member whose primary concerns are in scientific areas, one member whose primary concerns are in nonscientific areas, numerous members representing more than a single profession and demonstrating diversity, and at least one individual not affiliated with the institution. IRB Members may serve on one or more IRB Committees, and may or may not be assigned expedited reviews based on qualifications.

JCHR IRB Members are appointed by the Director of the HRPP in consultation with the IRB Chair(s). 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 patient advocate could serve as an alternate for another community-based patient advocate on another Committee.

The Director of the HRPP appoints the IRB Chairs and IRB Vice-Chairs. All IRB Members, including IRB Chairs and Vice-Chairs, are evaluated annually using an evaluation form, in accordance with JCHR HRPP/IRB Policies. The evaluation results will be provided to the Director of the HRPP. Written feedback will be provided to each IRB Member, and each member is encouraged to respond/comment on the form. (JCHR HRPP/IRB Policy Number 2011.01/01 – IRB Membership).

1.5 IRB Member Assignments

The IRB Administrator will instruct the IRB Coordinator(s) to assign a primary reviewer to each application that will be reviewed. For every 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 (e.g., personal emergency), the secondary reviewer will be able to serve as the lead to ensure that applications are not postponed due to no fault of the submission. When both the primary and secondary reviewers are present, then the secondary reviewer will focus on disagreement with the primary reviewer and/or additional comments to support the primary review. Submissions that are initially submitted for expedited review and then are brought before the full board for discussion (i.e., miscellaneous applications), 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 patient advocates) at a minimum, but all materials are available for review before, during and after meetings for all members via the web-based system, ***Jaeb.my.IRBManager.com*** (referred to herein as “IRBManager”). 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.

The JCHR IRB will be receiving submissions and notifications, performing reviews, corresponding with Sponsors and Sites, maintaining minutes, and providing review letters through IRBManager. All submissions must be made to the JCHR IRB via this 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.

With the efficiency of the new web-based system, the ***goal*** of the IRB is to have a response to the submitter of an application within one (1) week of receipt of a ***complete and correct*** submission for expedited reviews, within one (1) week after the full board meeting for non-expedited reviews, or within one (1) week of receipt of a translated document (see the section on Additional Provisions for Spanish-Speaking Subjects below for more information). The response could be the decision letter, or comments from the reviewer(s) requiring changes or clarifications. If changes or clarifications are required, then once received, the IRB will have an ***additional*** week to review said changes and provide a response to the submitter.

NOTE: If the IRB Coordinator(s) provide the preliminary administrative review and determine that an application is not complete or correct, they will not send that application to the reviewer(s). Incomplete or incorrect applications will be sent back to the submitter/Investigator for completion/correction first.

Any changes to an application that the IRB is requiring from the JCHR/Sponsor or Sites will be made through IRBManager. When the IRB Member(s) require edits, the system allows the IRB staff to provide a summary of changes, add comments/notes directly onto the application (xForm), 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. 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 (the email will say it is from "irbadmin@jaeb.org" specifically). (JCHR HRPP/IRB Policy Number 2018.07/01 – IRBManager).

1.5.1 IRBManager Access for JCHR/Sponsors and Sites

To submit applications (xForms) to or access JCHR IRB records, please visit ***Jaeb.my.IRBManager.com***. After initial registration (i.e., creating password, recovering password, etc.) you will be able to log in. Once logged in, there will be instructional materials and other resources available to users, including User Guides and Demos. Users will be given access to the appropriate protocols, under which users can submit applications (xForms). Users should be mindful of which types of xForms are submitted. Most JCHR/Sponsor applications will have "JCHR" in the title, and most Site applications will have "Site" in the title. The exceptions are applications that can be submitted by either JCHR/Sponsor or Sites, such as reporting events (e.g., Significant Deviations).

SECTION 2: IRB ACTIVITIES

2.1 Reviewing Research Activities

2.1.1 Initial Review of Research

All initial applications seeking to conduct human subjects research must be submitted through IRBManager for convened ("full board") review. This application may be reviewed as expedited if it qualifies, as confirmed by the assigned IRB Member, or may not be needed if it is determined to meet the exempt categorization, as confirmed by the assigned IRB Member (described herein). In accordance with the regulations, initial reviews will include the determination that all applicable requirements have been satisfied (see section on Criteria for IRB Approval of Research). Once approved, all research activities will be considered open and must comply with this Handbook until submitted to and approved by the IRB for final closure. (JCHR HRPP/IRB Policy Number 2001.08/02 – Initial Full Board Application).

2.1.2 Continuing Review of Research

This section sets forth the application submission requirements, circumstances that do not require standard continuing review, and criteria for IRB approval of continuing reviews for human subjects research. Once research has been approved, Continuing Review applications will be submitted for expedited or full board review respectively, at intervals appropriate to the degree of risk, but no less than once a year, unless, in accordance with the Final Rule provisions (Common Rule updates), the study meets the certain circumstances when a standard continuing review of research is not required. In general, a standard continuing review is not required for:

1. Research approved under an expedited review,
2. Research considered exempt that required only a limited IRB review (after the Final Rule goes into full effect), or
3. Research that 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 standard continuing review until study closure, even if the research has completed all interventions. ***NOTE: Once Sites have completed all research-related activities, they may submit to close their coverage with the IRB.***

The IRB may still choose to require a standard continuing review even if the criteria above are met, but the determination must be documented. For example, if the IRB has concerns about conflict of interest, noncompliance, or oversight, then the IRB can still require a standard continuing review. In the event that the IRB determines that standard continuing review is not required, the JCHR/Sponsors and Sites must still report amendments, qualifying adverse events, unanticipated problems, and deviations as required. To ensure that this documentation is established and to ensure that IRBManager extends the approval period for applicable studies, an abbreviated continuing review submission will be made no less than once a year so that the IRB can confirm that the study does not need a standard continuing review, or state why it does. Further, the JCHR IRB has the authority to observe or have a third party observe

the consent process and the research. (JCHR HRPP/IRB Policy Number 2001.08/03 – Continuing Reviews).

2.1.3 Amendments to Research Activities

The JCHR IRB requires that all changes ("amendments") to previously approved human subjects research be submitted through IRBManager for review. These applications may qualify for expedited review of minor changes or require full board review for major changes. Amendments may be submitted by the JCHR/Sponsor or by the Sites as applicable. Typically, Sites will amend the research-related activities at their Sites to incorporate Site-specific language into consent forms or add recruitment materials, which are often considered minor changes and will typically qualify for expedited review.

In accordance with the regulations, reviews of amendments will include the determination that all of the applicable requirements have been satisfied. (JCHR HRPP/IRB Policy Number 2001.08/04 – Submitting Amendments).

2.2 Ensuring the Rights, Safety, and Welfare of Human Subjects

The goal of the JCHR IRB is to ensure the rights, safety and welfare of the human subjects participating in JCHR led or conducted research. This goal starts with first reviewing the research (as previously stated), the Investigators conducting the research, and safety events related to that research.

2.2.1 Reviewing Site Investigators by Study

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 (i.e., Good Clinical Practice "GCP" training), FDA 483 Warning Letters, and gaps in practice (among other things). The JCHR IRB is responsible for assuring that Principal and Co-Investigators are appropriately qualified and capable in such a way that supports participation in the research for which they are seeking approval. 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 are responsible for any and all professionals delegated research-related activities on their behalf.***

(JCHR HRPP/IRB Policy Number 2015.03/03 – Investigator Qualifications). To evaluate competency for a particular research activity, the IRB reserves the right to require a delegation log, by study, for new Sites or Investigators. (JCHR HRPP/IRB Policy Number 2017.01/09 – Delegation Logs).

Site Investigators (i.e., Principal and Co-Investigators) applying for JCHR IRB approval may be asked to provide proof of licensure or board certification at the IRB's discretion. Supporting documents must be current and show a future expiration date or information that supports the expiration cycle. (JCHR HRPP/IRB Policy Number 2017.01/06 – Proof of Licensure).

Site Investigators seeking coverage with the JCHR IRB will need to include current CVs/Biosketches with applicable submissions for review of qualifications and appropriateness to work on each specified study. CVs/Biosketches for all JCHR staff are stored in the JCHR shared drive. (HRPP/IRB Policy Number 2013.11/07 – Updating CVs and Biosketches).

To document human subject's protection training, a Good Clinical Practice (GCP) training certificate must be submitted for JCHR IRB review, along with the Investigator's Attestation of the review and agreement to comply with this Handbook (see the JCHR IRB Investigator Handbook Attestation Form section herein). 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 a new application if these training requirements have not been completed.

Further, the Investigators will be evaluated for potential conflicts of interest as described in the section on Conflict of Interest Disclosure.

2.2.2 Reviewing Safety Events

The IRB is required to review the ongoing protections of human subjects. Examining events such as serious, related adverse events, unanticipated problems, and significant deviations contribute to the IRB's understanding of and confidence in the research being conducted. Event definitions and reporting expectations are described herein. Please note, as specified, the JCHR IRB may be required to provide additional reporting to the Office of Human Research Protections (OHRP), the Food and Drug Administration (FDA), and to local IRBs with whom the JCHR IRB has a reliance agreement.

2.3 Types of IRB Reviews

2.3.1 Exempt Qualification Reviews

The JCHR IRB may consider research activities involving human subjects conducted under the following categories "exempt" in accordance with 45 CFR 46 exemption categories. This includes:

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: **may only 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.).
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, if (*NOTE: may be applied to research involving children **if** the conditions of the exemption are met*):
    i. The human subjects are elected or appointed public officials or candidates for public office; or

ii. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

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.

NOTE: Per 45 CFR 46, the exempts above may only 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. (HRPP/IRB Policy Number 2010.10/02 – Exemptions and Secondary Research Activities).

2.3.2 Expedited Reviews

Reviews may be made without going to the full board during a convened IRB meeting. These reviews are known as Expedited Reviews. To be eligible for review 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 of 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 above for additional details)
   2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture (see the Notice 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 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, 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

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. Expedited review may be used for minor changes in previously approved research during the period in which approval is authorized. Minor changes such as the addition of Site-specific requirements that do not change the level of risk, 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 consent form into Spanish, etc.). Therefore, expedited review may be appropriate for the addition of recruitment or other subject materials that are ***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 review during a convened meeting. Further, specific changes required by the IRB may be approved via the expedited process without going to a fully convened board meeting.

Decisions regarding expedited reviews made by a primary reviewer (an experienced reviewer as designated by the IRB Staff under the supervision of the IRB Administrator) are: acknowledged, approved, approved with changes, and deferred. The IRB Members are informed of all expedited reviews via a report generated from IRBManager, which allows a date range of conducted reviews to be queried. All expedited review materials are available to the IRB Members via IRBManager. (HRPP/IRB Policy Number 2010.10/03 – Expedited Reviews).

2.3.3 Full Board Reviews

All human subjects research activities that do not meet the requirements for exempt categorization or expedited review will be submitted and reviewed by a fully 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: acknowledged, administrative hold, approved, approved with specific changes, deferred, not approved, and suspension. (HRPP/IRB Policy Number 2010.10/04 – Full Board Reviews).

Before the start of each convened meeting, the IRB Administrator (or 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 the discussion or vote on reviews for which they have a conflict. Verification of quorum will be recorded in the IRB meeting minutes along with the corresponding meeting's attendance. (HRPP/IRB Policy Number 2013.10/05 – Verification of Quorum).

2.3.3.1 Observation of IRB Meetings

Those who wish to attend a JCHR IRB meeting for general observation or training credits should contact the IRB office at least two weeks prior to the meeting via email at IRBadmin@jaeb.org. The schedule can be found as posted on the Intranet. The IRB needs advance notice to ensure there is adequate seating for all Board Members and guests. The IRB will notify the individuals making the request to inform them if they have permission to attend a specific session, or not, the week before the meeting.

Guests present for general observation must agree to the guest non-disclosure agreement. All guests must agree to the following:

- I WILL be on time for the meeting
- I will NOT take notes or have conversation during the meeting
- I will NOT have my phone, or any recording device, out during the meeting
- I will NOT discuss any votes taken during the meeting
- I will NOT disclose how IRB Members voted, and
- I will NOT discuss any details of any research discussed at the meeting.

Guests present for general observation must also agree to identify any research on the agenda for which they have a conflict of interest or are involved in as research staff and must agree to notify the IRB. Guests with a conflict will be asked to leave the room during the discussion and voting of those affiliated research activities. Additionally, guests looking to receive continuing education credit towards their certifications are required to stay for the full IRB meeting (except when excused due to conflict). A guest can attend any number of meetings per year with permission, but typically only two meetings can be counted towards continuing education credit. Certified staff requiring continuing education will have priority over non-certified staff. Lunch is

provided to the members only, so guests are encouraged to bring their own lunches to the meetings, as ***lunch is generally not provided to guests***.

At times, discussion of an IRB audit that has taken place or another sensitive issue is planned for the meeting agenda. On such occasions, the IRB may decide that the JCHR IRB needs to go into closed session for the discussion. When this happens, the IRB will ask all guests to briefly step out of the room so that the IRB can discuss the issue in a closed session.

2.4 Criteria for IRB Approval of Research

The criteria for IRB approval used by the JCHR IRB is defined in the Code of Federal Regulations and summarized below. The HHS regulations set forth the criteria for IRB approval of research in 45 CFR 46 (which are also consistent with the FDA regulations). These 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 following requirements are satisfied:

1. Risks to subjects are minimized:
    a. by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
    b. 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 provisions 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, 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.

(HRPP/IRB Policy Number 2010.10/05 – Approval Criteria).

2.5 IRB Documentation

As stated, for exempt and expedited submissions, one IRB Member is assigned to evaluate the submission as a "primary reviewer." If the submission will be going to the full board, then these submissions are assigned a primary reviewer, a "secondary reviewer," as well as other reviewers. All members are required to complete a corresponding reviewer checklist to verify and ensure all of the correct information is present and adheres to both federal regulations and policies and JCHR policies. The members not assigned as primary or secondary reviewers for full board meeting reviews will complete an abbreviated checklist as required. (HRPP/IRB Policy Number 2013.12/09 – Reviewer Checklists).

In addition to the documentation in the reviewer checklists, the JCHR IRB also takes meeting minutes, which demonstrate that the required elements of the fully convened IRB meetings are met. The required elements within the minutes include identifying 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. (HRPP/IRB Policy Number 2018.08/03 – Meeting Minutes and Controverted Issues).

2.5.1 IRB Requests for Modifications

The IRB Board (or IRB Expedited Reviewer) may require that changes or clarifications be made to protocols and corresponding materials in order to approve a particular submission. Wherever possible, the IRB will seek to make specific requests to improve understanding of expectations.

When the IRB Board 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, the IRB 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. In the event that the submitter and/or Investigator do not accept the changes made by the Board or reviewer, they may make additional proposals and these will be sent back to the IRB Board for full review at the next available convened meeting.

When the IRB Board requests non-specific changes or requires general clarifications (e.g., did you mean A or B, what is your process for… and how will you report it, etc.) the submitter and Investigator will be notified that the application has been deferred. The submitter and/or Investigator will then need to contact the IRB Office to request the Board's feedback. 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 Board at the next available convened meeting for review. At this time, the IRB Board 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 Board at a convened meeting, or whereby non-specific changes or clarifications will need to

go back to the IRB Board at a convened meeting. (HRPP/IRB Policy Number 2017.12/10 – IRB Requests for Modifications).

2.6 Approval Periods and Expirations

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 2001.08/04 Continuing Review, which allows the waiver of a standard continuing review, the studies will still be approved and extended 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

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 DSMB/DSMC reports that have not yet been submitted to the IRB (as applicable). 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. 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 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, including activities at the Site(s). If the response is inadequate or if one is not provided, then the IRB may take additional suspension or termination actions as described below.

(HRPP/IRB Policy Number 2014.02/01 – Approval Periods).

2.7 Suspension and Termination of IRB Approvals

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 for 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 ceding IRBs, the JCHR IRB may also need to report suspensions and terminations 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 decision letter will state the reason for suspension or termination and will identify any issues that have resulted in the suspension or termination. (HRPP/IRB Policy Number 2013.01/02 – Suspension and Termination Determinations).

SECTION 3: ETHICAL PRINCIPLES FOR THE CONDUCT OF HUMAN SUBJECTS RESEARCH

These principles, regulations, and guidance documents are incorporated herein as policies, procedures and instructions, and are essential for the ethical conduct of human subjects research. As such, all Investigators should be familiar with their requirements and recommendations as applicable. ***All of the regulations, guidance documents, and principles listed below are available on the Internet, and a browser search will easily identify original sources.*** Links are not provided herein as web-pages change and the links can quickly become irrelevant.

3.1 The Belmont Report

The Belmont Report was developed by the National Commission of the Protection of Human Subjects of Biomedical and Behavioral Research. It states that there should be clear boundaries between practice and research, and states that there are three basic principles that guide how human subjects research is to be conducted:

- ***Respect for Persons*** – this principle essentially states that people should be treated as autonomous individuals capable of making their own decisions and choices, and shall be able to do so, and where a person is unable to do so (i.e., diminished capacity) the individual is still entitled to protection
- ***Beneficence*** – this principle essentially states that we must first do no harm when conducting research (i.e., justifiable risks), and second, we must maximize the possible benefits while minimizing the potential harms when conducting research (i.e., risk-benefit-ratio)
- ***Justice*** – this principle essentially states that, when dealing with research, there should be a fairness or equality among subjects. For example, not only should individuals in a particular group not be unfairly targeted because they are a vulnerable or "easy" population to recruit, but also individuals in a particular group should not be left out of research activities that could benefit them or their group. The burden and benefit of research participation should be distributed (i.e., social justice)

3.2 The Declaration of Helsinki

The Declaration of Helsinki was developed by the World Medical Association and establishes the principles for the conduct of medical research involving human subjects. There are five (5) overarching principles for the conduct of human subject research:

- ***Beneficence and Nonmaleficence*** – this principle essentially states that there are moral and scientific boundaries that must be upheld in the conduct of research and it is unethical and not in the best interest of the human subjects to newly experiment without a solid foundation for the experiments (i.e., background information and justification for research activity, not just "hey let's see what happens if…")
- ***Fidelity and Responsibility*** – this principle essentially states that research-related activities should be conducted by qualified Investigators and delegated staff who uphold professional standards of conduct

- ***Integrity*** – this principle essentially states that ethical and professional, as well as social, norms should be upheld when conducting human subjects research
- ***Justice*** – this principle essentially states that there should be fairness and equality among human subjects selected for research
- ***Respect for People's Right and Dignity*** – this principle essentially states that all individuals have a right to dignity, privacy, confidentiality, and self-determination (i.e., control over one's own life)

3.3 Health and Human Services (HHS) Regulations

These regulations apply to the conduct of human subjects research that is funded or supported by a federal agency (e.g., the National Institutes of Health). The sources of these regulations are regularly updated, so please use an internet search engine to find the current regulations using the key terms provided below under ***45 CFR 46 – Protection of Human Subjects***:

- Subpart A: The Common Rule
- Subpart B: Protections for Pregnant Women
- Subpart C: Protections for Prisoners
- Subpart D: Protections for Children

3.4 Food and Drug Administration (FDA) Regulations

These regulations apply to the conduct of human subjects research activities that fall under the purview of the FDA (i.e., drug and device studies) as stated under the following (among other regulations):

- 21 CFR 50: Protection of Human Subjects
- 21 CFR 54: Financial Disclosure by Clinical Investigators
- 21 CFR 56: Institutional Review Boards
- 21 CFR 312: Investigational New Drugs
- 21 CFR 812: Investigational Device Exemptions

3.5 Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rules

As stated, the JCHR HRPP/IRB requires that human subjects research activities comply with the HIPAA privacy rules as stated under the following regulations (and several guidance documents):

- 45 CFR 160: General Administrative Requirements
- 45 CFR 162: Administrative Requirements
- 45 CFR 164: Security and Privacy

3.6 Good Clinical Practice (GCP)

The JCHR HRPP/IRB requires that human subjects research activities comply with the principles of Good Clinical Practice as described in the following guidance documents as promulgated by the FDA and HHS:

- ICH E6 (R2): Good Clinical Practice (JCHR also complies with the recommendations in ISO 14155:2011 Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice as incorporated in JCHR policies and procedures)

SECTION 4: GENERAL KNOWLEDGE

4.1 What is Research?

4.1.1 HHS Criteria

According to 45 CFR 46 (as applicable to any research regulated by a Federal department or agency), ***Research*** is defined 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, that is planned to be in full effect approximately 20 Jan 2019, whereby ***Human Subject*** means "a living individual about whom an investigator (whether professional or student) conducting research:

1. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
2. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens."

Also under the 2019 changes to 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."

4.1.2 FDA Criteria

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)).

4.2 What isn't Research?

Although certain research activities are considered exempt (see section on Exempt Qualification Reviews), other activities are not research at all, and/or do not involve human subjects, and so do not need to comply with these requirements. As such, these activities are not submitted and reviewed by the IRB. An example would be a training initiative where staff are trained on the use of a device that is marketed, and can wear that device if they so choose, but an Investigator would not be collecting data to contribute to generalizable knowledge from that device use, and the trainee would not be considered a human subject.

4.3 Who does the JCHR IRB Consider an Investigator?

In general, an ***Investigator*** is an individual performing various tasks related to the conduct of human subjects research activities. The Office of Human Research Protections (OHRP) interprets an Investigator to be any individual who is involved in conducting human subjects research studies. Such involvement would include:

- Obtaining information about living individuals by intervening or interacting with them for research purposes
- Obtaining identifiable private information about living individuals for research purposes
- Obtaining the voluntary informed consent of individuals to be subjects in research, and
- Studying, interpreting, or analyzing identifiable private information or data for research purposes

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

The JCHR IRB considers Investigators to be in one of the following categories:

- ***JCHR/Sponsors*** – these individuals may be Investigators per OHRP, but may or may not actually be conducting the research as a Site (e.g., Sponsor-Investigator).
- ***Site Principal Investigators*** – these are the individuals that are responsible as the leader of the team conducting the research at a Site (i.e., ultimately responsible for the conduct of research at the Site under this research). Principal Investigators are responsible for all staff, even Sub-Investigators, to whom they have delegated responsibilities.
- ***Site Co-Investigators*** – these individuals are as equally responsible for the oversight of the research at a Site as the Principal Investigator (i.e., "Co-Principal Investigators"). Co-Investigators are usually designated when there is one institution, but more than one physical location that requires oversight (e.g., two offices).
- ***Site Sub-Investigators*** – these individuals may conduct activities and have responsibilities as delegated by the Principal Investigator, but are not responsible for the overall conduct of the study at the Site (e.g., they can still perform physicals, conduct consent, dispense medications, perform procedures, etc. as qualified, trained, and delegated).

4.4 What are the Responsibilities of an Investigator?

The Investigator must always follow the investigational plan of a research activity, federal regulations, IRB requirements and instructions, and Good Clinical Practice. Investigators are responsible for obtaining IRB approval before beginning any human subjects research activity. Investigators are responsible for providing the IRB with sufficient information and related materials about the research (e.g., research protocols, consent documents, etc.) so that the IRB can fulfill its regulatory obligations, including making the required determinations. Investigators are responsible for the conduct of anyone working on their behalf as delegated for a given research activity. Additional responsibilities are as follows.

4.4.1 Compliance

Along with meeting the specific requirements of a particular research activity, Investigators are responsible for ongoing requirements in the conduct of approved research that include, in summary:

- Obtaining and documenting informed consent and HIPAA authorization of subjects or subjects' legally authorized representatives prior to the subjects participation in the research, unless these requirements have been waived by the IRB
- Obtaining prior approval from the IRB for any amendments of the previously approved research, including amendments to the informed consent process and document, except those necessary to eliminate apparent immediate hazards to subjects
- Ensuring that progress reports and requests for continuing review and approval are submitted to the IRB in accordance with the policies, procedures, and actions of the IRB
- Providing the IRB with prompt reports of any unanticipated problems involving risks to subjects or others
- Providing the IRB with prompt reports of significant deviations or noncompliance with the regulations or the requirements or determinations of the IRB
- Providing the IRB with prompt reports of serious, related adverse events
- Keeping certain records as required by the HHS regulations for at least three (3) years after completion of the study, or as required by the FDA regulations for at least two (2) years post completion or withdraw of a Premarket Application (or confirmation that there will not be one), and as required by the HIPAA privacy rule for at least six (6) years after the collection/use of Protected Health Information

Further, additional responsibilities can be found in Good Clinical Practice as promulgated by the FDA, which include:

- The researcher *should* inform the subject's primary physician about the subject's participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed
- Although a subject is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher *should* make a reasonable effort to ascertain the reason for withdraw, while fully respecting the subject's rights

4.4.2 Conflict of Interest Disclosure

JCHR has specific requirements for defining, training, reporting, and managing conflict of interest (COI) for JCHR as an institution; for JCHR staff on an annual basis; for the JCHR IRB Members; and for Principal and Co-Investigators submitting for coverage of the JCHR Institutional Review Board per research study (in accordance with the policy described below). The policy and corresponding procedures are intended to support JCHR's compliance with 42 CFR 50 Subpart F; 21 CFR 50, 54, and 56; 45 CFR 46; and the standards set forth by the Association for the Accreditation of Human Research Protections Program (AAHRPP) by whom the JCHR HRPP is accredited. This compliance serves to demonstrate how JCHR ensures that the design, conduct and reporting of JCHR research is free from bias resulting from conflicts as described, in accordance with JCHR HRPP/IRB Policy 2017.01/04, which states:

Investigators working on Public Health Services (PHS) funded research and/or Food and Drug (FDA) regulated research will need to report financial disclosures to the JCHR Principal Investigator/Project Director ("PI/PD" per PHS regulations) and/or the JCHR Protocol Director when JCHR is the Sponsor or the delegated Contract Research Organization (CRO). This reporting will be done prior to the receipt of funding or start of the study, annually (for PHS funded studies), and as changes to potential conflicts arise (within thirty (30) days of the

change) during the course of the study and for one (1) year following the completion of the study.

Site Principal and Co-Investigators seeking coverage by the JCHR IRB must submit complete and correct conflict of interest disclosure forms with their Site Addition to Protocol submissions for each protocol, any time there is a change to the Principal or Co-Investigator's potential conflicts (within thirty (30) days of the change), and will provide any applicable updates not previously reported during the submission of the Site's annual reviews. All Principal and Co-Investigators submitting for coverage to the JCHR IRB are trained via the review and attestation to this JCHR IRB Investigator Handbook. Specific definitions and instructions are provided on the actual disclosure forms. Training on conflicts of interest disclosures is required every four (4) years, however as training is provided within this handbook, it will occur no less than every three (3) years.

In addition, Sites working on federally supported studies with JCHR may use the JCHR Conflict of Interest SOP to train and follow at their Site when they do not have their own policy and procedures implemented (i.e., private practices). Where Sites follow the SOP, they will provide training documentation and conflict reporting to the applicable JCHR PD/PI. The JCHR PD/PI will then review and manage the conflicts on behalf of the Sites (instead of the Director of the HRPP who reviews and manages conflicts for JCHR Staff/IRB Members).

All JCHR employees are required to submit conflict of interest disclosure forms upon hire, annually thereafter, and any time there is a change to the employee's potential conflicts (within thirty (30) days of the change).

JCHR IRB Members must submit conflict of interest disclosure forms upon acceptance as a member, annually, and any time there is a change to the member's potential conflicts (within thirty (30) days of the change). All JCHR staff members (and IRB Members) are required to review and sign-off on the Conflict of Interest SOP to document training on the JCHR policy and procedures for conflict of interest.

4.4.3 Human Subjects Protection Training

The JCHR IRB adapts the National Institutes of Health (NIH) requirement for training in the protection of human subjects. As such, all Principal Investigators and Co-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 can be found herein. The material covered in this Handbook also addresses the role of the HIPAA Privacy Rule in the research environment. All JCHR/Sponsor Investigators, as well as JCHR Protocol Managers and Monitors, and Site Principal and Co-Investigators must complete training on this 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 current JCHR IRB Investigator Handbook. The JCHR IRB will accept GCP training from any institution that is also accepted by the NIH. Some institutions may require their Investigators to complete training that is not considered GCP Training to fulfill their institutional requirements. This training will also be accepted by the JCHR IRB if a reliance agreement is in place. 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. (HRPP/IRB Policy Number 2011.04/02 – Human Subjects Protection Training).

4.4.4 IRB Submissions

All submitters must ensure that all applications (xForms) and their supporting documents are complete upon submission via ***Jaeb.my.IRBManager.com*** ("IRBManager"). Principal Investigators are also required to sign off on the applications (xForms) to attest to completion and accuracy. IRBManager 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 a car was uploaded). If the IRB Coordinator determines that a submission is incomplete or incorrect, then the IRB Coordinator will send the application back to the submitter and/or Investigator for completion/correction. Once a final, complete and correct application is received, then an IRB Coordinator will assign the application to the IRB Member(s) for review 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 activity has been approved. Further, if the JCHR/Sponsor is requesting an amendment, Sites cannot submit updates to local materials to reflect/incorporate the changes in that amendment until after that 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.

SECTION 5: RELIANCE AGREEMENTS

The JCHR IRB recognizes that the NIH released a policy on the use of a single Institutional Review Board for multi-site research, notice number: NOT-OD-16-094, which starts the process to offer IRB review as a Single IRB for JCHR coordinated studies (Effective new date: September 25, 2017). IRBs may rely on each other to fulfil the requirement of a single IRB through the use of a reliance agreement.

From the NIH definition, "A ***reliance agreement*** is a formal, written document that provides a mechanism for an institution engaged in research to delegate institutional review board (IRB) review to an independent IRB or an IRB of another institution." Institutions may call these agreements by different names (e.g., reliance agreement, IRB authorization agreement (IAA)). Agreements may cover single studies, categories of studies, or all human subjects research under an organization's Federalwide Assurance (FWA). (HRPP/IRB Policy Number 2016.06/02 – Single IRBs).

A Site that has oversight by a local IRB can request JCHR IRB coverage under the following conditions:

1. 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).
2. A reliance agreement must be executed prior to JCHR IRB submission for the addition of the Site under a study.
3. 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.

Sites that do not have a local IRB may submit to the JCHR IRB without any additional action (HRPP/IRB Policy Number 2012.03/01 – Site Coverage by JCHR IRB).

SECTION 6: IMPORTANT DEFINITIONS

6.1 Serious Adverse Events (SAEs)

There is required reporting and managing of adverse events for studies overseen by the JCHR IRB. In accordance with the identified regulations and guidance documents for Good Clinical Practice, the JCHR IRB uses the adverse event related definitions found in the JCHR SOP CT 202 – Adverse Event and Device Reporting (described herein).

Sites are required to report all ***serious, related*** adverse events in any human subjects research activity, regardless if the event was expected/anticipated, to the IRB 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*** application (xForm) via IRBManager.

Further, if the ***JCHR/Sponsor*** believes that an event in an IND study qualifies as ***serious, related, 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 JCHR/Sponsor must notify the FDA (and Investigators) as soon as possible but no later than seven (7) calendar days after the JCHR/Sponsor's initial receipt of the information. ***The JCHR IRB will still be notified within seven (7) calendar days of the identification of any event as a SUSAR, even events that were not fatal or life-threatening.***

For IDE studies, the ***JCHR/Sponsor*** must report any ***serious, related, unanticipated device effects (UADEs)*** to the FDA, all reviewing IRBs, and participating Investigators within ten (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 qualifying UADE.***

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

To ensure that both the Site Investigator and the JCHR/Sponsor fulfill their obligations, the IRB may receive two notices if an event has occurred at a JCHR IRB covered Site. One notice from the Site Investigator that states an event was serious and related, and then if the JCHR/Sponsor determines the event is a SUSAR or UADE, another notice about the same event from the JCHR/Sponsor.

Adverse events that are not serious, related adverse events need only be submitted as a log in the continuing review submission by the JCHR/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 should specify which Sites are JCHR IRB Sites in their report/log where possible. For other unanticipated problems that do not meet the definition of an adverse event, please see the following section titled "Unanticipated Problems." (HRPP/IRB Policy Number 2001.08/06 – Adverse Events).

6.2 Unanticipated Problems (UPs)

Consistent with the OHRP Definitions, 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.

Sites are responsible for reporting all unexpected instances that are possibly related to participation in the research within seven (7) calendar days of recognition. These unexpected instances shall be submitted via IRBManager by completing an ***Adverse Event/Unanticipated Problem Reporting*** application (xForm).

JCHR/Sponsors must also report all unexpected instances not directly involving a specific Site that are possibly related to participation in the research within seven (7) calendar days of recognition. These unexpected instances shall also be submitted via IRBManager by completing an ***Adverse Event/Unanticipated Problem Reporting*** application (xForm). 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 in general, 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, FDA, or other funders accordingly. Additional reporting by the JCHR IRB to a local IRB may be required under terms of the reliance agreement. (JCHR HRPP/IRB Policy Number 2014.09/06).

6.3 Significant Deviations and Noncompliance

This section provides definitions of applicable deviations and noncompliance, and describes the process for reporting and managing noncompliance as applicable.

Deviation: Any action that departs from the established policies and procedures, formal documents or processes (e.g., statistical analysis plan), Good Clinical Practice, federal or state laws, or regulations applicable to the conduct of research.

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, or safety of the research subjects, or negatively influences the scientific study integrity.

The JCHR IRB requires immediate reporting (within seven (7) calendar days) of all significant deviations, any deviations to eligibility or study treatment, and

noncompliance relating to JCHR research. The Sites shall submit events that occurred at the Site, and the JCHR/Sponsor shall submit events not applicable to a specific Site. These submissions will be made via IRBManager using the Significant Deviation/Noncompliance Reporting application (xForm).

Any situation, incident, or process during the conduct of human subject research that is inconsistent with ethical standards, project policies, federal or state laws, or regulations applicable to the research study may be considered noncompliance. An incident may be considered noncompliance regardless if there was an increased risk to subject rights, safety, or welfare, or data integrity. Some examples include deviations to informed consent, eligibility criteria, and investigational product usage, but this is not a comprehensive list. When 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 subjects' rights, safety or wellbeing, or pose a risk to the integrity of the study or data?"

Informed Consent Example: If an informed consent form stamp did not print, but the entire process was conducted and documented correctly on the correct version of the consent form, then there would not appear to be a risk to the subjects' rights. If however, the subject did not sign the consent form to attest to the conduct of the consent process, then can it be said that:

1. "Legally effective consent" was obtained before involving the subject in research (if not, then the deviation presented a risk to the subject's rights), and
2. The Investigator followed the IRB requirements of informed consent documentation

If both of the above are not confirmed, then this would be reported immediately as a significant deviation, even if the subject's signature was obtained at a later date as a corrective action. ***NOTE: Action can be taken by the IRB to stop research activities due to noncompliance.*** Please see section on Suspension and Termination of IRB Approvals for more information. Further, in accordance with the reliance agreements established with ceding IRBs, the JCHR IRB may also need to report noncompliance of Sites to local IRBs.

6.4 Research Misconduct

In accordance with JCHR HRPP/IRB Policy Number 2017.12/14 – Research Misconduct: Each institution that applies for or receives funding from the federal government for research or other related activities must identify, manage and report research misconduct allegations under such research related activities. According to 42 CFR 93.103, ***Research Misconduct*** means:

1. Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results
    a. fabrication is making up data or results and recording or reporting them
    b. falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record
    c. plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit

NOTE: Research misconduct does not include honest error or differences of opinion.

In order to be a finding of research misconduct as described above, the following must have been demonstrated as identified during the inspection of the allegation:

1. There was a significant departure from accepted practices for the relevant research community;
2. The misconduct was committed intentionally, knowingly, or recklessly; and
3. The allegation can be proven by a preponderance of the evidence.

The main responsibility for the receipt, evaluation and investigation of allegations of research misconduct and reporting of investigational findings falls to the Director of the HRPP for JCHR. Once the investigation has been completed, a copy of the official report must be sent to the IRB Office. The IRB Members will determine if IRB coverage is suspended or not 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 may have specific reporting requirements. ***NOTE: Action can be taken by the IRB to stop research activities due to misconduct.*** Please see section on Suspension and Termination of IRB Approvals for more information.

Further, in accordance with the reliance agreements established with ceding IRBs, the JCHR IRB may also need to report possible misconduct at Sites to local IRBs. The local IRBs will be responsible for investigating and managing the misconduct for their Site staff in accordance with their local policies and procedures, but the JCHR IRB can still suspend or terminate the JCHR IRB approval of their research.

6.5 Undue Influence

Any attempt or instance of undue influence toward the IRB must be reported to the Director of the HRPP (hrpp@jaeb.org). 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 to the Director of the HRPP. (JCHR HRPP/IRB Policy Number 2014.06/03 – Undue Influence).

SECTION 7: INFORMED CONSENT AND HIPAA

7.1 General Informed Consent Information

All informed consent and assent templates can be found on the JCHR website. The Adult, Parental, and Adult/LAR ICFs must be written at an 8th grade reading level wherever possible. Please note that in order for the IRB stamp of approval to be used on the informed consent form, the margins must be set according to the current JCHR consent template and providing 1 inch in the upper right corner of the header, follow template guidelines for font size, format, and instructions for footers, and ***must be submitted to IRBManager in a word or PDF format***. The templates contain a placeholder of where the stamp will appear. Neglecting to adhere to the template and guidelines can delay your stamped documents. ***Note: All protocol materials should also adhere to these margins.***

7.2 Legally Authorized Representatives (LARs)

7.2.1 LARs for Adults Lacking Capacity to Consent

In accordance with Florida 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 JCHR IRB will only permit, in the following order, (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 (*NOTE: The order is important, so if for example the adult has a court appointed guardian, then their child cannot serve as their LAR).*

7.2.2 LARs for Minors

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
- Legal Custodians or Legal Guardians
- Emancipated Minor (if self)

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

7.3 Minors in Research

When research involves minors (children), the IRB follows the requirements in Subpart D of 45 CFR 46 and 21 CFR 50 pertaining to approving an assent process for children, obtaining assent of children, and permission/consent of the legally authorized representative. If a minor, who is currently enrolled in a JCHR IRB approved protocol, ***turns seven (7) 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 LAR will be

required to attest to the process in the assent document. As with any research, the Investigator may request a waiver or other modification of the assent requirement for IRB consideration. (HRPP/IRB Policy Number 2015.02/01 – Assent Requirements).

If a minor, who is currently enrolled in a JCHR IRB approved protocol, ***turns eighteen (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 research, the Investigator may request a waiver or other modification of the consent requirement for IRB consideration. (HRPP/IRB Policy Number 2015.02/02 – Turning of Age Consent).

7.4 Elements of Informed Consent

The following are the basic elements that are required to be included in the informed consent:

Basic Element 1:

- A statement that the study involves research
- An explanation of the purposes of the research
- The expected duration of the subject's participation
- A description of the procedures to be followed
- Identification of any procedures which are experimental

Basic Element 2:

- A description of any reasonably foreseeable risks or discomforts to the subject

Basic Element 3:

- A description of any benefits to the subject or to others which may reasonably be expected from the research

Basic Element 4:

- A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject

Basic Element 5:

- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained

Basic Element 6:

- For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained

Basic Element 7:

- An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject (Research, Rights, Injury Qs)

Basic Element 8:

- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled

Basic Element 9:

- One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
    - A statement that identifiers might be removed from the identifiable private information of identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another Investigator for future research studies without additional informed consent from the subject or LAR, if this might be a possibility, or
    - A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies

Additional elements are required when appropriate and may include one or more of the following elements to be provided in informed consent:

Additional Element 1:

- A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable

Additional Element 2:

- Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's or the legally authorized representative's consent

Additional Element 3:

- Any additional costs to the subject that may result from participation in the research

Additional Element 4:

- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject

Additional Element 5:

- A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject

Additional Element 6:

- The approximate number of subjects involved in the study

Additional Element 7:

- A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit

Additional Element 8:

- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions

Additional Element 9:

- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

Broad consent may be permitted as an alternative to the informed consent requirements above, when there is a plan to use broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, then the following elements of broad consent are incorporated into the informed consent (as soon to be required under the revisions to the Common Rule, the JCHR IRB has already incorporated):

Broad Consent Element 1:

- The information required in the Basic Elements 2, 3, 5 and 8, and when appropriate, Additional Elements 7 and 9

Broad Consent Element 2:

- A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted

Broad Consent Element 3:

- A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens

Broad Consent Element 4:

- A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite)

Broad Consent Element 5:

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

Broad Consent Element 6:

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

Broad Consent Element 7:

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

NOTE: In October 2017 the NIH executed a policy that states that institutions must include the Certificate of Confidentiality statement in the consent forms for NIH funded studies (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html). The policy specifically states: "For studies in which informed consent is sought, NIH expects Investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy."

When submitting a consent form to IRBManager, Investigators must ensure that at least two forms of each version are submitted. One form must have ***all changes/edits to the form tracked in Word*** from the appropriate template or previous version, and the other form must be the clean copy, with all edits accepted, also in Word. If the IRB reviewer discovers that only some edits have been tracked and others have not, then the reviewer may send the application back to the submitter/Investigator for correction before completing the review. To ensure that there are not unnecessary delays due to inconsistencies, please be sure to ***track all changes*** during the consent writing process and accept all changes for a clean copy prior to submitting.

7.5 The Consent Process

Unless otherwise authorized or waived by the IRB (if legally permissible), it is the Investigators' responsibility to obtain written informed consent and HIPAA authorization (that have been approved by the JCHR IRB) from each subject or the subject's LAR. Investigators must be present to complete the consent process and obtain HIPAA authorization, and are responsible for assuring that the written informed consent:

1. Is in the language and format approved by the IRB
2. Is obtained under circumstances that offer the subject or the representative sufficient opportunity to consider whether or not to participate
3. Contains the signature and signature date of the subject or the subject's legally authorized representative (if legally permissible)
4. Is signed and dated by the Investigator his/herself as evidence that informed consent was obtained (except where permitted below in the section on Signature Requirements).
5. Fully signed copy has been given to the subject or the subject's legally authorized representative, and
6. Process was completed prior to the conduct of any and all research-related procedures, including data collection.

The IRB will evaluate, among other items already described, the steps taken to minimize the possibility of coercion or undue influence towards subjects. Coercion occurs when one person to another intentionally presents an overt or implicit threat of harm in order to obtain compliance. However, coercion can be more subtle. For example, an Investigator enrolling his child into a significant risk device study as a participant may be considered coercion. Undue influence often occurs through an offer of an excessive or inappropriate reward or other overture in order to obtain compliance. For example, if a Site wants to offer minors in a study a $50.00 iTunes gift card for each completed visit, in addition to the IRB approved stipend for all subjects/LARs, then this could be considered coercive, as the amount paid directly to a seven year old for example, might be a lot of money.

7.6 Documenting Informed Consent

In accordance with the HHS and FDA regulations, informed consent must be documented for human subjects research activities, unless a waiver or alteration is granted by the JCHR IRB. This policy describes the instances and methods that are used to provide this documentation in accordance with the regulations.

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; 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 communications throughout the course of the study must also be in their native language. (JCHR HRPP/IRB Policy Number 2014.02/02 – Documenting Informed Consent).

7.6.1 Signature Requirements

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, as approved by the IRB.

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) a designee of the Investigator on the research staff may sign the consent form to attest to the process, as approved by the IRB.

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, as approved by the IRB.

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, as approved by the IRB. *NOTE: This research may require shorter continuing review periods (e.g., six (6) months instead of a year).*

NOTE: The IRB reserves the right to require more than one LAR signature on any consent form and/or require an Investigator signature on any consent form where the IRB determines that the additional requirements improve human subject protections. (JCHR HRPP/IRB Policy Number 2018.08/02 – Consent Form Signatures).

7.7 Additional Provisions for Spanish-Speaking Subjects

Spanish-speaking subjects must be consented with the JCHR IRB approved translated consent form. A qualified Spanish interpreter (i.e., someone other than a relative or friend, etc.) must be present for the entire consent form process, must sign the consent form at the time that the Investigator and subject/LAR sign it, and their qualifications should be documented in a consent note. Further, the Investigator(s) must ensure that the Spanish-speaking subject/LAR has someone who is Spanish speaking available anytime by phone or in person to answer questions or concerns for all study related interactions, including office visits.

JCHR IRB has contracted Spanish Solutions of Tampa, LLC for all requested Spanish translation services, however, other translators may be used as long as a Certificate of Translation is provided. To submit an approved English document (consent forms, assent forms, participant materials, etc.) for Spanish translation, the study team should submit the request on the ***Miscellaneous Submission*** application (xForm) via IRBManager. The request for translation may be reviewed via expedited review. The submission should include the Request for Spanish Translation Form signed by the JCHR Investigator (when using Spanish Solutions), the JCHR IRB approved and stamped English versions of each document being translated, and all documents to be translated (in Microsoft Office Word format). The Word documents should have highlighted, in Yellow, all sections to be translated to Spanish. Only sections highlighted will be translated and charged for services. When the application is received with the correct materials attached, the IRB administrative staff will send the materials to Spanish Solutions for translation (as applicable). While the materials are being translated, the application will remain under “Administrative Review” in IRBManager. When the translated documents and final invoice

are received, the IRB administrative staff will upload the materials to complete the submission and will then assign the application to an IRB Member for review. Due to the nature of the translation process and need for IRB approval, these applications will typically take longer than others to be assigned.

The JCHR IRB Office will provide the Spanish translated templates of informed consents and assent for research staff, therefore, template language will not be charged to the study team unless altered. Incomplete sentences and specific words or phrases cannot not be requested for translation, only whole sentences and paragraphs. *NOTE: The JCHR IRB does not require main study informed consent forms to be translated to Spanish if they will not be used by multiple Sites. If Sites will be using their own Site-specific consent forms, submissions can be made to request translation of those approved forms instead. JCHR/Sponsors may decide to translate the main study consent form and submit Site-specific consent sections to save on cost if multiple Sites will require Spanish materials.*

7.8 Waivers/Alterations of Informed Consent/HIPAA

This section describes what constitutes activities that may qualify for a waiver or alteration of consent or HIPAA provisions, clarifies when such requests for waiver or alteration may be made, and what JCHR HRPP/IRB requirements must be met relating to these activities. Any request for a waiver or alteration of consent and/or HIPAA provisions may be submitted via IRBManager by completing the designated fields in the ***JCHR/Sponsor New Study*** application (xForm) or the ***JCHR/Sponsor Study Amendment*** application (xForm). These activities may be reviewed using the expedited review procedure depending on the nature of the change.

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/HIPAA language omitting some or all elements of informed consent, for research-related activities if:

1. The research activity involves no more than minimal risk;
2. The research activity could not be 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.

(JCHR HRPP/IRB Policy Number 2017.12/11 – Requests for Waiver/Alteration of Consent/HIPAA).

7.9 Preparatory to Research Activities (Partial HIPAA Waiver)

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 request for Preparatory to Research activities. 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 IRBManager via the ***Site Addition to Protocol*** application (xForm) or the ***Site Amendment to Research Activities*** application (xForm). 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.

7.10 Consent Form and HIPAA Amendments and Addendums

An ***amendment*** is a change to a consent form, and an ***addendum*** is the addition of material(s) to supplement a consent form. Addendums should not repeat, or conflict with, the content in the main document, particularly as it relates to informed consent because it can be confusing for the subjects/LARs.

In line with these definitions, ***JCHR/Sponsors*** can create ***amendments*** to consent forms to add, remove, or correct the content of an approved consent form. For example, if the protocol was updated to change the number of study visits, then the consent form would be amended to also reflect this change. JCHR/Sponsors can submit ***addendums*** when there is new information that does not change or restate the content of the approved consent form, but would be new information that would be important for the existing subjects to have.

Also in line with these definitions, ***Sites*** can submit ***amendments*** when they need to add Site-specific language (e.g., a new section about genetics required by their state law), or when the Site-specific language is different from what has been approved (e.g., Site provides emergency care for study-related injuries). Sites shall not make amendments to the study-specific content, unless required. Further, Sites can submit ***addendums*** to the approved consent forms to add material that support the consent form. For example, the Site may require a separate form for a state's Bill of Rights, or may even require a separate HIPAA form.

When a Site-specific addendum is used (i.e., a separate form) the following must be met:

1. The consent form shall reference the additional addendums/forms
2. Where the provisions are covered in the consent form, they shall be removed (e.g., remove redundant HIPAA language from consent form if a separate HIPAA form will be used), and
3. The Site must get JCHR IRB approval of these addendums/forms prior to use in the applicable study.

SECTION 8: OTHER SUBJECT MATERIALS

Other subject materials include any and all materials that are provided or presented to the subjects/LARs (e.g., recruitment materials). Both the HHS and the FDA consider recruitment materials to be part of the informed consent process (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/clinical-trial-websites/index.html). The FDA "considers direct advertising for study subjects to be the start of the informed consent and subject selection process. Advertisements should be reviewed and approved by the IRB as part of the package for initial review. However, when the clinical investigator decides at a later date to advertise for subjects, the advertising may be considered an amendment to the ongoing study. When such advertisements are easily compared to the approved consent document, the IRB chair, or other designated IRB Member, may review and approve by expedited means, as provided by 21 CFR 56.110(b)(2). When the IRB reviewer has doubts or other complicating issues are involved, the advertising should be reviewed at a convened meeting of the IRB" (https://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm).

IRB approval is required for all written or printed materials (e.g., recruitment flyers, questionnaires, brochures, letters, etc.) that will be provided or presented to study subjects/LARs regarding the study activities or study results. Study information displayed on public websites and social media are included in these categories requiring review and submissions shall contain the complete draft of the message to be posted, and the public URL for the IRB to view where the final content is to be displayed. In addition, IRB approval is required for the presentation of study results on a public website as reviewed in the informed consent forms.

Certain materials that are publically available and have not been created for the purposes of a given study do not need IRB approval (i.e., user guides for a marketed device that anyone can access even if they are not in a study). If study-developed scripts are produced, such as radio ads or instructional videos, the wording must first be approved by the IRB (submitted as an amendment to research materials on IRBManager), and then ***the actual produced recording must be submitted*** for IRB approval or acknowledgement prior to running also (submitted via the ***Miscellaneous Submission*** application (xForm) on IRBManager). For example, a radio script will be IRB approved, and then produced, and then the produced audio will need to be submitted for IRB approval or acknowledgement.

All subject materials to be used during the course of the approved research study are to be submitted for approval from the IRB prior to dissemination and use. ***NOTE: Submitting recruitment materials for approval is not the same thing as submitting for approval of certain recruitment activities that would be considered "preparatory to research."*** Please see the Preparatory to Research Activities section herein for more information.

Some of the information that the IRB is assessing, to ensure that there is not a risk to subjects rights, during review of subject/LAR recruitment materials includes, but is not limited to, the following:

- Is the material understandable to the intended audience
- Is the material consistent with the approved consent form/language
- Does the material appear to be making promises, such as statements or implications of a certainty of favorable outcome or other benefits beyond what is outlined in the consent document

- Has any exculpatory language been included
- Does there appear to be an emphasis of payment or other benefits (e.g., free supplies)
- Is there promise of “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation
- Are there claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling (as applicable)
- Are terms used, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational
- Is there language that could be interpreted as making potential subjects feel guilty or disadvantaged if they don’t go into the study (e.g., “Is it time to start taking your health seriously?”)
- Is there language that could be interpreted as a scare tactic to get potential subjects to participate in the study (e.g., “Not taking care of your disease could lead to serious problems, even death. Are you ready to start taking care of yourself?”)

NOTE: A good tip for creating recruitment materials is to use language that is consistent with the IRB approved consent forms. The JCHR/Sponsor may submit for review of recruitment materials that can be used by the JCHR/Sponsor and/or the Sites as attachments to the ***JCHR/Sponsor New Study Submission*** application (xForm) or the ***JCHR/Sponsor Study Amendment*** application (xForm) via IRBManager. Sites can also submit for review of recruitment materials that are specific to the Site at attachments to the ***Site Addition to Protocol*** application (xForm) and the ***Site Amendment to Research Activities/Materials*** application (xForm) via IRBManager. (JCHR HRPP/IRB Policy Number 2014.07/05 – Approval of Subject Materials).

SECTION 9: JCHR/SPONSOR NEW RESEARCH SUBMISSIONS

9.1 New Study

When the JCHR/Sponsor is submitting to the IRB to have a new protocol or research activity reviewed by the JCHR IRB, the JCHR/Sponsor will submit the ***JCHR/Sponsor New Study Submission*** application (xForm) in IRBManager. (For information about how to complete applications, please visit the "*Notices"* section that looks like a post-it note of your IRBManager main page (dashboard) for instructions provided in the link called "*JCHR/Sponsor IRBManager Demo")*. This submission (xFor will be completed when the JCHR IRB will be overseeing the overall conduct of the research, regardless of each Sites' intent to apply for coverage under the JCHR IRB. This submission will be made when the JCHR/Sponsor does not believe that the research would qualify as Exempt (see section on Exempt Qualification Reviews for more information). These submissions may qualify for expedited review or may require a full board review depending on the nature of, and risk associated with, the research. For more information regarding expedited reviews, please see the Expedited Reviews section.

This xForm may be submitted for everything from drug/device studies to simple surveys. IRBManager uses smart forms so only questions applicable to the kind of research you are doing will appear for completion. For example, if you say the study is a survey only, then questions required for drug/device studies will not be populated for completion. *NOTE: These submissions will need to contain the study-related materials that are intended to be used at the time of the submission. For example, questionnaires, instructional video scripts, etc. referenced in the protocol or application, must be reviewed with the original application.* ***Submissions made referencing materials that are not provided will be sent back to the submitter/Investigator and will not be reviewed.*** For JCHR-specific research activities where the overall research was submitted separately for review/approval by an external IRB, but JCHR is just performing a specific function, the application in the next section shall be used (i.e., Scientific Engagement Only).

9.2 Scientific Engagement Only

When JCHR will be scientifically engaged in a research-related activity, but will not be submitting to the JCHR IRB for overall coverage of the actual research project, then the ***JCHR Scientific Engagement Only New Study Submission*** application (xForm) in IRBManager will be submitted. This would be for studies that already have Sponsor-obtained IRB approval, where Sites have IRB approval (or will have separate approval), but JCHR is simply getting JCHR IRB approval for their specific activity involvement. For example, if JCHR will be performing data analysis only. The JCHR IRB will only be reviewing JCHR's roles and responsibilities under this submission, and as such, should always qualify for expedited review (i.e., JCHR's role on previously approved research presents no more than minimal risk, and would qualify as a minor change).

The JCHR Scientific Engagement Only New Study Submission xForm will also be used when a funder requires initial IRB approval of a proposal for the sake of obtaining a grant, but only when actual research studies will be submitted individually for review/approval by an IRB. For example, the 123 Foundation requires approval of the YesMa'am network, but each protocol under the YesMa'am network grant will be submitted separately for IRB approval. The JCHR

IRB considers these submissions to qualify for expedited review to fulfill the requirement of the funder and is neither greater than minimal risk, nor research (as actual research studies will be reviewed separately).

SECTION 10: JCHR/SPONSOR AMENDMENTS, CONTINUING REVIEWS, AND CLOSURE OF RESEARCH

10.1 Amendments to Research

The JCHR/Sponsor is required to submit all amendments to research activities or study materials for review/approval prior to implementation and/or dissemination to Sites. This includes updates to questionnaires and new general recruitment materials, such as the addition of a recruitment flier that all Sites can use. All subject materials to be used during the course of the approved research study are to be submitted for approval from the IRB prior to use.

The JCHR/Sponsor will log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***JCHR/Sponsor Study Amendment*** application. The submission may or may not qualify for expedited review (see section on Expedited Reviews for more information). The JCHR/Sponsor will receive notification in writing from the IRB that the requested amendment has been reviewed and will include the decision by the IRB. The research expiration date will continue to correspond to the current continuing review date, or one (1) year after initial approval, unless otherwise determined to be changed by the IRB. Sites working on JCHR/Sponsor research that are overseen by the JCHR IRB will submit their Site-specific changes and materials separately.

Where the JCHR IRB has reviewed and approved JCHR to perform scientific engagement activities only, and another IRB is (or IRBs are) responsible for the actual protocol and research activities, then the JCHR team need only submit amendments that will modify JCHR's duties and responsibilities specifically. The JCHR/Sponsor will log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***JCHR/Sponsor Scientific Engagement Only Amendment*** application.

10.2 Continuing Review of Research

Continuing Review applications of previously approved human subjects research will be submitted at intervals appropriate to the degree of risk, but no less than once a year. The JCHR/Sponsor will log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***JCHR/Sponsor Study Continuing Review*** application or the ***JCHR Scientific Engagement Only Continuing Review*** application (for studies approved initially as applicable). For more information about what activities might qualify for shorter review periods, please see the section under IRB Activities, Continuing Review of Research. The IRB will notify the JCHR/Sponsor of upcoming expiration of research activities 90, 60, 30, 7, and 1 day(s) prior to the expiration date. Please note that any submission (even if previously approved as expedited) may be sent to the full board, and full board submissions may require clarifications or deferral to the next full board meeting. For this reason, it is highly recommended that ***submissions for continuing review are made in time to (1) allow for the expedited submission to be seen at a full board meeting prior to the expiration date, and (2) allow for the full board submission to be seen at second full board meeting prior to the expiration date***, just in case there are questions or a deferral is made. Do not assume that the IRB will be able to squeeze in a last

minute application, or will not perform an adequate review, just because the research is about to expire or lapse in coverage.

If IRB coverage lapses, no new subjects can be enrolled and no study data can be collected until IRB approval is obtained. This includes activity at the Sites. It will be the JCHR/Sponsor's responsibility to ensure compliance. No research activity shall occur until the JCHR/Sponsor has received written notification from the IRB office that the protocol continuing review application has been approved by the IRB.

There may be instances where a standard continuing review is not required, in which case an abbreviated submission may be made. In these cases, the same application (xForm) will be used, but the JCHR/Sponsor can indicate that it meets the requirements of an abbreviated submission and the form will only populate the items required for this type of submission (this automatically requests a waiver of standard continuing review). For more information about this continuing review waiver, please see the section under IRB Activities, Continuing Review of Research.

10.3 Closure of Research Activities

This procedure sets forth the research protocol final application submission requirements and procedures for the review process. All Sites with approval to conduct research under a given protocol must close coverage 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. The JCHR/Sponsor will log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***JCHR/Sponsor Study Closure*** application or the ***JCHR Scientific Engagement Only Closure*** application (as applicable).. Once the IRB has approved closure, no additional research related activities can be conducted. (JCHR HRPP/IRB Policy Number 2001.08/05 – Submitting for Closeout).

SECTION 11: SITE ADDITION TO RESEARCH, AMENDMENTS, CONTINUING REVIEWS, AND CLOSURE OF ACTIVITIES

11.1 Adding a Site to JCHR/Sponsor Approved Research

Sites can only be added to a research activity after the JCHR/Sponsor has obtained approval for that research. For Sites that have a local IRB, they can also only be added once a reliance agreement has been established between JCHR IRB and the local IRB (see the Reliance Agreements section herein).

In IRBManager, the following steps must be followed to be added to the research:

1. The JCHR/Sponsor research is approved
2. At least one person from the Site is registered in IRBManager (i.e., has set up a password), as they will need to complete the xForm – this is usually going to be the primary Site Coordinator
3. The Site Principal Investigator (PI) is registered in IRBManager *(NOTE: Where Site PI is used in IRBManager it is referring to the Investigator at the Site that will be taking direct responsibility for the oversight of the study – IRBManager does not use group or network level roles/titles)*
4. The JCHR/Sponsor starts the ***Site Addition to Protocol*** application to add the Site to their specific research, and will use the email of the registered Site personnel to send the application for completion
5. The Site personnel will receive the application (called an ***xForm*** in IRBManager) by way of an email from ***IRBAdmin@jaeb.org***
6. The Site personnel will either click the link in the email to login and complete the xForm, or can go into ***jaeb.my.IRBManager.com*** anytime to access their xForms (i.e., applications)
7. Site personnel will complete the xForm and will need to enter at least the Site Principal Investigator's email as it appears in the IRBManager system (remember the Site PI must already be registered as noted above). All other Site personnel needing to be added to the study will also need to be pre-registered in IRBManager
8. The xForm will then go to the Site PI by way of email from IRBAdmin@jaeb.org, or they can login directly to jaeb.my.IRBManager.com and the application can be found under "xForms awaiting your attention" on the main dashboard
9. Once the Site PI reviews, confirms and signs off, then the form is considered submitted to the JCHR IRB

Instead of having multiple applications, the Site shall include the following in this initial submission:

- Requests for Preparatory to Research activities (Partial HIPAA Waivers)
- Site-specific consent modifications (custom consent)
- Site-specific recruitment materials (optional)

- Investigator qualification materials (CVs/Biosketches, GCP Training, Conflict of Interest Disclosure Forms, JCHR IRB Investigator Handbook Attestations, etc.)

Only complete and correct applications will be assigned to the IRB Member(s) for review. Applications (xForms) that are not complete and correct will be sent back to the personnel that made the submission and Site Principal Investigator for correction/clarification by the IRB Administrative Staff. For more information about how to complete applications, please visit the ***Notices*** section that looks like a post-it note of your IRBManager main page (dashboard) for instructions provided in the link called ***Site IRBManager Demo***.

11.2 Site Amendments to Research Activities

During the conduct of the research, once the Site has been approved, there may be additional changes that need to be made by the Site. These changes will typically occur when (1) the Site wants to add new or updated materials (e.g., a new recruitment flier), or (2) when the Site has a custom consent form and the JCHR/Sponsor has amended the main consent forms, and so now the Site needs to update their custom consents. The Site can log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***Site Amendment to Research Activities/Materials*** application. Please note, when Sites are submitting amendments to incorporate the changes from the main research, these applications cannot be submitted until the JCHR IRB has already approved those main study changes.

NOTE: In IRBManager, when there is a main study consent change, and after a Site has received approval for their initial Site-specific changes, the site will need to submit to incorporate those main changes into their approved consent version. For example, the JCHR/Sponsor submitted consent form version 1.0, then the site submitted their Site-specific changes and received approval. Now, the JCHR/Sponsor has received approval for consent form version 2.0, then the Site must submit to add the version 2.0 JCHR/Sponsor changes to their previously approved Site-specific consent form (containing the original version 1.0 and Site-specific language).

11.3 Site Continuing Reviews

Sites must submit no less than once a year for a review of their activities under a particular research project. For more information about what activities might qualify for shorter review periods, please see the section under IRB Activities, Continuing Review of Research. The IRB will notify the Site of upcoming expiration of research activities 90, 60, 30, 7, and 1 day(s) prior to the expiration date by way of an email from ***IRBAdmin@jaeb.org***. The Site can click the link in the automated email in order to be brought directly to the appropriate research project page, click the "Start xForm" link on the left side of the screen, and then select the applicable xForm, the ***Site Continuing Review of Research Activities*** application. This submission can also be started manually by logging into IRBManager (***jaeb.my.IRBManager.com***), selecting the research project they wish to update (under "My Projects"), and then proceeding to the Start xForm link on the left side of the screen to begin the appropriate xForm.

Please note that any submission (even if approved previously as expedited) may be sent to the full board, and full board submissions may require clarifications or deferral to the next full board meeting. For this reason, it is highly recommended that ***submissions for continuing review are made in time to (1) allow for the expedited submission to be reviewed at a full board meeting prior to the expiration date if the application becomes deferred from expedited***

review, and (2) allow for the full board submission to be seen at a second full board meeting prior to the expiration date, just in case there are questions or a deferral is made. Do not assume that the IRB will be able to squeeze in a last minute application, or will not perform an adequate review, just because the research is about to expire.

If IRB coverage lapses, no new subjects can be enrolled and no study data can be collected until IRB approval is obtained. It will be the Site PI's responsibility to ensure compliance. No research activity shall occur until the Site has received written notification from the IRB office that the protocol continuing review application has been approved by the IRB.

There may be instances where a standard continuing review is not required, in which case an abbreviated submission may be made. The same application will be used, but the Site can indicate the request for waiver of standard continuing review. For more information about this continuing review waiver, please see the section under IRB Activities, Continuing Review of Research.

11.4 Site Closure of Research Activities

Upon completion of the Site's activities under a given research project, the Site can log into IRBManager (***jaeb.my.IRBManager.com***), select the research project they wish to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then select the applicable xForm, the ***Site Closure of Research Activities*** application. Once the Site has received approval from the IRB that they are closed, then they cannot perform any additional research activities related to that project. The Site cannot close their research activities if there are still active subjects in the study at their Site.

11.5 Emergency Use Notifications

The JCHR IRB does not plan to provide coverage for emergency use of investigational product (drugs/devices). In the event however that a JCHR IRB covered Site Investigator has used investigational product without adequate informed consent ***solely to sustain the life of a person***, then the Site Investigator must report this use, and include 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 by logging into IRBManager (***jaeb.my.IRBManager.com***), selecting the research project to update (under "My Projects"), select the "Start xForm" link on the left-hand side of their screen, and then selecting the ***Emergency Use Notification*** application (xForm). 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.

(JCHR HRPP/IRB Policy Number 2017.12/13 – Emergency Use).

11.6 Sub-Investigators Not Listed

As stated herein, the JCHR IRB does not require the reporting and tracking of Sub-Investigators as they are performing Investigator roles as delegated on behalf of a Principal Investigator (PI). That PI has responsibility for the oversight of all personnel as delegated, including Sub-Investigators. Sites who notice a sub-Investigator is not listed in IRBManager or request to have all investigators listed on their IRB approvals can contact the JCHR IRB at irbadmin@jaeb.org to add the sub-Investigators.

If a Principal or Co-Investigator would like to be re-assigned to become a Sub-Investigator, this cannot be handled via email and must submit a ***Miscellaneous Submission*** application (xForm).

SECTION 12: SITE AND JCHR/SPONSOR SUBMISSIONS

12.1 Adverse Events and Unanticipated Problems

Adverse events may encompass both physical and psychological harms. They occur most commonly in the context of drug or device research, although on occasion, they can occur in the context of social and behavioral research as well (e.g., highly sensitive questions triggered an emotional break). Submissions can be made by logging into IRBManager (***jaeb.my.IRBManager.com***), selecting the research project to update (under "My Projects"), selecting the "Start xForm" link on the left-hand side of their screen, and then completing the applicable xForm, the ***Adverse Event/Unanticipated Problem Reporting*** application. As serious adverse events may or may not also be unanticipated problems, this one application allows for the reporting of both (or either). See sections under Important Definitions, Serious Adverse Events and Unanticipated Problems herein for more information on definitions used by the JCHR IRB.

Sites are responsible for reporting all ***serious, related adverse events*** involving risks to subjects and others (expected or unexpected) to the JCHR IRB within seven (7) calendar days of identification of the event. Sites will follow the prompts on the xForm for "***Site Reporting***" or other similar prompts. Sites will also report unanticipated problems that have occurred at the Site on this application in the same required timeline.

JCHR/Sponsors are responsible for reporting all ***SUSARs and/or UADEs***, as well as unanticipated problems occurring at the JCHR/Sponsor or vendors, or other systemic events. The JCHR/Sponsor is required to report within seven (7) calendar days of the Sponsor's determination that the event qualifies as such. The JCHR/Sponsor will follow the prompts on the xForm for "***JCHR/Sponsor Reporting.***"

NOTE: One event may need to be reported twice, (1) by the Site as a qualifying serious, related adverse event, and then (2) by the JCHR/Sponsor once it is determined that the event qualified as a SUSAR or UADE. Remember, there are two reporting requirements here, one by the Site and one by the JCHR/Sponsor.

12.2 Significant Deviations and Noncompliance

The JCHR IRB requires immediate reporting (within seven (7) calendar days) of all significant deviations and noncompliance relating to JCHR research activities. For definitions and examples, please see the Significant Deviations and Noncompliance section under Important Events above. It is important to note that any situation, incident, or process during the conduct of human subject research that is inconsistent with ethical standards, project policies, and federal or state laws or regulations applicable to the research study may be considered noncompliance. An incident may be considered noncompliance regardless if there was an increased risk to subject rights, safety, or welfare, or data integrity (e.g., a willful action). Significant deviations and/or noncompliance will be made by logging into IRBManager (***jaeb.my.IRBManager.com***), selecting the research project to update (under "My Projects"), selecting the "Start xForm" link on the left-hand side of their screen, and then completing the applicable xForm, the ***Significant Deviation/ Noncompliance Reporting*** application.

Sites will complete the application to report a significant deviation or noncompliance that occurred at the Site. Sites will follow the prompts on the xForm for "***Site Reporting***" or other similar prompts.

The ***JCHR/Sponsor*** will complete the application to report a significant deviation or noncompliance that is not directly related to a specific Site (e.g., system malfunction lead to incorrect randomization assignments). The JCHR/Sponsor will follow the prompts on the xForm for "***JCHR/Sponsor Reporting***" or other similar prompts. The JCHR/Sponsor may hold and report non-significant deviations on the continuing review submission, which requires a report of all deviations (both significant and non-significant).

12.3 Miscellaneous Submissions

Miscellaneous Submissions are broad xForms that can be used for submitting requests that do not seem appropriate for any other xForm application, such as for Spanish translations, Personnel Changes, or DSMC Memos. Miscellaneous submissions can be reviewed via Full Board or expedited review depending on content and request. The JCHR/Sponsor and the Sites can submit Misc xForms by logging into IRBManager (***jaeb.my.IRBManager.com***), selecting the research project they wish to update (under "My Projects"), selecting the "Start xForm" link on the left-hand side of their screen, and then completing the applicable xForm, the ***Miscellaneous Submission*** application. ***Note: The JCHR/Sponsor will use the JCHR/Sponsor Miscellaneous Submission xForm and the Sites will use the Site Miscellaneous Submission xForm.***

If 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. (JCHR HRPP/IRB Policy Number 2013.11/06 – Unexpected Leave of Principal Investigator).

SECTION 13: JCHR IRB INVESTIGATOR HANDBOOK ATTESTATION FORM

By signing this form, I, _____ (print full name),

attest that I have completely read, understood, had the opportunity to ask questions concerning the JCHR IRB Investigator Handbook, and will abide by its contents. This includes training and compliance with the following as specified in this version of the JCHR IRB Investigator Handbook:

- Ethical Principles for the Protection of Human Subjects
    - The Belmont Report
    - The Declaration of Helsinki
- The Code of Federal Regulations (as identified herein)
- Good Clinical Practice requirements (separate documentation required)
- Financial Conflict of Interest (and disclosure requirements)
- JCHR HRPP/IRB Policies and Procedures

I understand my responsibilities as an Investigator conducting research, and know that I am ultimately responsible for the activities conducted by individuals designated to work on studies under my oversight as Investigator. I understand that my JCHR IRB coverage is contingent upon me adhering to all applicable regulations, the requirements of the JCHR HRPP/IRB, and Good Clinical Practice. If for any reason, I do not adhere to these regulations and requirements, my JCHR IRB coverage may be placed on hold, suspension, or termination without warning.

Signature: _____ Date: _____

Name of Institution: _____

(Principal Investigators employed at JCHR will complete sign off through the JCHR Document Management App.)