

Investigator Manual

Spectrum Health IRB Policies and Procedures

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What is the purpose of this manual?

The Investigator Manual is designed to guide you through policies and procedures related to the conduct of Human Research that are specific to Spectrum Health. General information regarding Human Research protections and relevant federal regulations and guidance is incorporated into the required human protections training. For additional information on the training see the question below: “What training do my staff and I need in order to conduct Human Research?”

What is Human Research?

The organization considers activities to be “Human Research” when they meet the Department of Health and Human Services (DHHS) regulations definition at 45 CFR §46.102(d) and 45 CFR §46.102(f) and/or the Food and Drug Administration (FDA) regulations definition at 21 CFR §56.102(c), 21 CFR §56.102(e), and 21 CFR §812.3(p). An algorithm for determining whether an activity is Human Research can be found in the “CHECKLIST: Human Research Determination,” located in the IRB Member Forms section of the HRPP website. Further guidance, the “IRB Guidance Document on Quality Improvement Activities vs. Research”, located in the IRB Policies and Guidance section of the HRPP website is available to assist researchers in distinguishing human research activities. In addition, the U.S. Agency for International Development (USAID) has a guidance document posted on its website “Protection of Human Subjects in Research Supported by USAID” dated 12/26/2006 that provides examples (e.g. outbreak investigations, journalism, criminal investigations, etc.) of activities that would not meet the definition of human subject research requiring IRB review and approval. Use these documents for guidance as to whether an activity meets either the DHHS or FDA definition of Human Research, keeping in mind that the IRB makes the ultimate determination in questionable cases as to whether an activity constitutes Human Research subject to IRB oversight.

How do I determine if my project requires IRB approval?

You cannot conduct Human Research as defined by the DHHS and FDA regulations without prior IRB review and approval, or a formal determination the Human Research is exempt or does not qualify as Human Subject research (e.g. quality improvement). For more information on the exempt determination, see the question “What are the types of IRB Review?” further below in this manual. Utilize the “CHECKLIST: Human Research Determination” located in the IRB Member Forms section of the HRPP website and/or “IRB Guidance Document on Quality Improvement Activities vs. Research” located under the IRB Policies and Guidance section of the HRPP website if you are unsure if your research meets the DHHS and FDA regulations definition of Human Research. If you have questions about whether an activity is Human Research per the regulations, submit an application for a formal determination to the IRB office prior to starting any project-related activities.

What is the Human Research Protection Program?

A Human Research Protection Program is an organization’s overall plan to protect subjects participating in Human Research. The “Spectrum Health Human Subject Protection Program Overview” document located on the IRB Policies & Procedures section of the HRPP website describes Spectrum Health’s HRPP program. It includes the program’s mission, ethical principles, applicable laws, when the organization is engaged, and the organization’s role and responsibilities.

What training do my staff and I need in order to conduct Human Research?

Investigators and staff must complete the online Collaborative Institutional Training Initiative (CITI) human subject protections training program prior to the submission of their research for IRB review. The CITI website can be accessed at <http://www.citiprogram.org/>. This training is valid for a three-year period, after which a Refresher CITI Course must be completed to continue conducting Human Research at Spectrum Health. For additional information on the CITI training requirements, review the “Education (CITI Info)” section of the HRPP website.

Investigators and staff are required to complete and pass the Basic Biomedical Course. Upon completing the course, a certificate of completion and the cumulative score will be sent electronically by CITI administration to the IRB office. It is your responsibility to print and retain a valid paper copy of the completion certificate for your records. If you have completed the CITI course at another institution, you will need to log in to the CITI website and affiliate yourself with Spectrum Health. For additional information on registering and affiliating in CITI, review the “Education (CITI Info)” section of the HRPP website.

All members of the research team are required to complete this mandatory ethics training. IRB approval will not be granted for protocols in which research team members have not completed human research protections training under the Spectrum Health affiliation.

Spectrum Health as an institution, the IRB, the Sponsor, and/or funding agency may also require additional training and /or credentials in order to conduct the research depending on the Sponsor and/or the type of research.

How do I write a Research Protocol?

A protocol is a detailed plan of why the research is being done and how it will be conducted. Typically, the sponsor of the Human Research will provide the protocol. If you are an investigator sponsoring or leading your own Human Research, you are expected to create and submit a protocol for the IRB to review. You may use the “TEMPLATE: Human Research Protocol” to assist you in protocol development and writing. This template includes the sections at a *minimum* the IRB expects to see included. Here are some key points to remember when developing a protocol:

- The “TEMPLATE: Human Research Protocol” serves only as guidance to investigators when developing a Human Research Protocol for submission to the IRB. Remove the italicized instructions on what to include (e.g. *Describe the purpose, specific*) from your final protocol. If you are a new investigator, it is strongly recommended that you work with a faculty advisor or mentor in developing your protocol.
- When writing a protocol, always keep an electronic copy of the final IRB approved protocol. You may need to modify this copy and submit it to the IRB with tracked changes, if future amendments/changes need to be made. Update the version date with each modification to the protocol.
- Depending on the nature of your research (e.g. retrospective chart review), certain sections of the protocol template (e.g. data safety monitoring) may not be applicable. Remove sections that are not applicable to your type of Human Research.

How do I create a consent document?

The informed consent form provides the potential subject important information to consider before deciding whether or not to participate in the Human Research. Typically, the sponsor of the Human Research will provide a sample informed consent document. You are expected to ensure the sponsor-provided informed consent document has the required elements per regulations, has local contact information, includes IRB suggested language and, for clinical trials, includes Good Clinical Practice required items. If you are not

working with a sponsor or a sample informed consent document is not provided, you will need to create an informed consent document. You may use the “Informed Consent Template” located under the IRB Forms section of the HRPP website to assist you in consent development and writing.

Prior to submitting the informed consent document to the IRB, refer to “Required Elements of Informed Consent and HIPAA,” located under the IRB Forms on the HRPP website to ensure all required elements are present. Please note depending on the type of research and the level of risk, not all sections of the informed consent document are applicable. For example, the section addressing what will or will not be covered if a research injury occurs is not required for minimal risk research. In addition, slight variations in the informed consent form wording are permitted to better reflect the research (i.e. the word “study” can be changed to “registry” or “biorepository”). However, it is recommended to adhere as closely as possible to the exact informed consent template wording to ensure all required elements and statements are met for approval.

You must date your informed consent document to ensure that you use the most recent version approved by the IRB when consenting subjects. Always keep an electronic copy of the final IRB approved consent document. You may need to modify this copy and submit it to the IRB with tracked changes, if future amendments/changes need to be made. Update the version date with each modification to the consent.

Once the IRB has approved your informed consent form, it will be stamped in the bottom right corner with the date of the IRB approval and the last date the document can be used. This stamped informed consent form must be the one used to obtain informed consent and must be signed by the research participant.

If you have questions on creating your informed consent document or other related consent documents such as assent documents, short forms, information sheets or telephone scripts, please contact the IRB office for assistance at irbassist@spectrumhealth.org or (616) 486-2031.

How do I determine if my research requires HIPAA authorization?

The federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA) requires authorization (permission) from the subject to be obtained to access, use or share identifiable health information for research purposes. Alternatively, a waiver from this requirement may be granted for the Human Research by the institution’s Privacy Board if certain regulatory criteria are met. The Spectrum Health IRB has a dual role and also serves as the Research Privacy Board.

The DHHS Office for Civil Rights defines when the health information is considered identifiable under regulation 45 CFR §164.514(b) and the criteria that must be met to permit a waiver of authorization 45 CFR §164.512. If your Human Research will access, collect or share any of the listed identifiable items with the subject’s health information and you do not meet the criteria for a waiver of authorization, you will be expected to include a HIPAA authorization to participate in the Human Research. This can be a standalone authorization or incorporated into the consent form. To request a waiver of HIPAA authorization, select this option during the completion of the initial IRB application.

If you need to create a HIPAA authorization document, start with the “Informed Consent Template” which contains the HIPAA authorization towards the end of the document. This template can be found under the IRB Forms section of the HRPP website. Even though it is not required, it is recommended to combine the consent and HIPAA authorization into one document.

Verify the HIPAA authorization contains all the required elements prior to submission for review by the IRB. Reference the worksheet “Required Elements of Informed Consent and HIPAA”, located under the IRB Forms on the HRPP website.

How do I submit the initial IRB application?

All initial applications are submitted to the IRB electronically via a secure website designed by IRB Manager. The website address is <https://spectrumhealth.my.irbmanager.com>. You can also access the website via our IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> or by entering the key word “IRB Manager” into any search engine (i.e. Google).

Upon entering the IRB Manager website, you will be prompted to enter your user name, password, and client name. The client name is “spectrumhealth” as one word. If you forget your password, select “Forgot Password?” from the log in screen to have a new password sent to your email address. If you need a username and password, or become locked out, email irbassist@spectrumhealth.org to have a username and password sent to you or to have your account reset.

For step-by-step instructions on how to fill out the initial IRB application please see the next question “How do I complete the initial IRB application?”.

How do I complete the initial IRB application?

For step-by-step instructions on how to fill out the initial IRB application please reference the following documents on our IRB website <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> “How to get to the xform you need” and “Quick reference for signing a document in IRB manager”. These documents can be found on our website under the item “Electronic Submission”. If you have questions when completing the form online, please initially reference the document “IRB Manager FAQs”. If your question is not addressed or you run into any problems, you can call the Office of the IRB at 616-486-2031 or email irbassist@spectrumhealth.org and we will be happy to assist you.

How do I request a waiver from the informed consent requirement?

On your initial IRB application indicate you are requesting a waiver for this question. Please be aware, the FDA regulations in general do not permit waiver of informed consent to be granted except in rare situations involving emergency research, emergent life-threatening situations, and in research with the armed forces. The DHHS regulations 45 CFR §46.116 and 45 CFR §46.117 permit the IRB to grant a waiver or alteration of informed consent requirement if certain conditions are met.

How do I submit a Humanitarian Use Device application to the IRB for review?

If you are using the Humanitarian Use Device (HUD) consistently with FDA approved labeling for medical treatment, then complete an “Initial Application for IRB Review” form, located under the IRB Forms (Start xForm) section of the IRB Manager website. For the question asking about research type, be sure to select “HUD”.

Please note if you are using a Humanitarian Use Device (HUD) consistent with the FDA approved labeling, you are NOT required to submit a research informed consent document with your application for IRB review. However, you are expected to include a copy of the patient information or brochure that will be provided to the patient describing the device and the potential risk and benefits.

If you are using the HUD as part of a research study evaluating the safety and effectiveness of the device, this request will be reviewed by the convened IRB as a typical device study. In the “Initial Application for IRB Review,” for the question research type, select “All other research studies.” Do not select “HUD,” as this will take you through the wrong version of the initial application.

Is there an application fee for IRB submissions?

The IRB office will invoice a fee for all industry sponsored (research sponsored by for-profit organizations) study submissions, continuing review, and protocol modifications requiring expedited or convened IRB review. The initial submission fee for convened review is \$2000 and \$1500 for expedited review. All continuing reviews and substantial modifications requiring expedited or convened IRB review are \$500.

Invoices are sent following the IRB meeting in which the study is reviewed and payment is due 45 days from receipt.

As an investigator, you are responsible for ensuring these fees are covered in your Clinical Trial Agreement with the sponsor.

What are the types of IRB Review?

Submitted activities may fall under one of the following types of IRB review:

- **Not “Engaged”:** DHHS Office of Human Research Protections (OHRP) defines an institution as *engaged* in human research when its employees or agents for the purposes of the research obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research. For example, if a Spectrum Health physician collects a blood sample for a genetic research study being conducted at another institution and has the informed consent obtained by the other institution and does not collect data about the subject for the research then Spectrum Health would not be considered engaged in the Human Research. Contact the IRB Office in cases where it is unclear whether or not you are *engaged* in Human Research.
- **Not “Human Research”:** Activities must meet the DHHS or FDA definition of “research” involving “human subjects” for the activity to fall under IRB oversight. Activities that meet neither definition of “Research” involving “Human Subjects” are not subject to IRB oversight or review. Review the IRB Office’s “CHECKLIST: Human Research Determination” for reference. Contact the IRB Office in cases where it is unclear whether an activity meets the regulatory definition of Human Research.
- **Exempt:** Certain categories of Human Research may be exempt from regulation but require IRB review. It is the responsibility of the IRB, not the investigator, to determine whether Human Research is exempt from IRB review. Review the IRB Office’s “CHECKLIST: Exemption Determination” for reference on the categories of research that may be exempt. Human Research determined to be exempt does not require continuing review by the IRB.
- **Review Using the Expedited Procedure:** Certain categories of non-exempt Human Research may qualify for review using the expedited procedure. Reference the categories of research that may be reviewed using the expedited procedure per DHHS OHRP guidance available at: <http://www.hhs.gov/ohrp/policy/expedited98.html>.
- **Review by the Convened IRB:** Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

What is the typical turnaround time on IRB review?

Turnaround time on a submission varies depending on the 1) the type of submission (e.g. initial reviews typically take longer to review than modifications to previously approved research) 2) the completeness and accuracy of the submission (e.g. missing information and/or forms delay processing) 3) if the submission requirements are met (e.g. CITI training completed for listed research personnel) 4) the complexity of the request and 5) the current IRB office workload at the time of submission.

The IRB generally convenes for meetings two times a month. Expedited review occurs on an ongoing basis.

The IRB office processes thousands of requests each year. Their goal is to process these requests in a timely manner. If four weeks or more have passed since your submission, and you have not received correspondence from the IRB office, please feel free to contact the IRB office for a status update at irbassist@spectrumhealth.org or (616) 486-2031. Be sure to include the investigator's last name, protocol name, IRB # (if known) and approximate date of submission in your inquiry.

What are the decisions the IRB can make when reviewing a protocol?

The IRB may approve research, require modifications to secure approval, table research, defer, or disapprove research:

- **Approval:** Made when all criteria for approval are met. See the question "How does the IRB decide whether to approve Human Research?" below.
- **Modifications Required to Secure Approval:** Made when IRB members require specific modifications to a protocol before approval can be finalized.
- **Tabled:** Made when the IRB cannot approve the research at a meeting for reasons unrelated to the protocol, such as loss of quorum. When taking this action, the IRB automatically schedules the protocol for the next meeting.
- **Deferred:** Made when the IRB determines that the board is unable to approve a protocol and the IRB suggests modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in person or in writing.
- **Disapproval:** Made when the IRB determines that it is unable to approve a protocol and the IRB cannot describe modifications that might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

How does the IRB decide whether to approve Human Research?

The IRB follows the federal regulations published by the Department of Health and Human Services (DHHS) and the Food and Drug Administration (FDA). These regulations define the criteria to be met in order to approve research. Reference [45 CFR 46.111](#) for the DHHS criteria for approval and [21 CFR 56.111](#) for the FDA criteria for approval.

What happens after IRB review?

The IRB will provide you with a written decision indicating that the IRB has approved the Human Research, requires modifications to secure approval, has deferred, or has disapproved the Human Research.

- **If the IRB has approved the Human Research:** The Human Research may commence once the IRB letter of approval and the IRB-stamped informed consent form are received and all other organizational approvals have been met. IRB approval is good for a limited period of time, not to exceed one year. This approval period is noted in the approval letter.

- If the IRB requires modifications to secure approval and you accept the modifications: Make the requested modifications and submit them to the IRB within 30 days using the “Modifications Required to Secure Approval of Human Research” form, located under Start xForm on the left side of the study protocol screen on the IRB Manager website. If all requested modifications are made, the IRB will issue an approval letter. Research cannot commence until this approval letter is received. If you do not respond to the IRB within 30 days, the offer of approval with the requested modifications may be withdrawn. If you do not accept the modifications, write up your rationale for not accepting the modifications on the “Modifications Required to Secure Approval of Human Research” form, and submit it to the IRB within 30 days. If you do not provide additional information or correspondence within 30 days, the IRB may withdraw your submission and require a new protocol submission.
- If the IRB defers the Human Research: The IRB will provide a statement of the reasons for deferral and suggestions to make the study approvable, and give you an opportunity to respond in writing. If you do not provide additional information or correspondence within 30 days, the IRB may withdraw your submission and require a new protocol submission.
- If the IRB disapproves the Human Research: The IRB will provide a statement of the reasons for disapproval and give you an opportunity to respond in writing. If you do not respond within 30 days, the IRB may require a new protocol submission.

In all cases, you have the right to address your concerns (appeal) to the IRB directly at an IRB meeting.

What are my obligations after IRB approval?

- 1) Do not start Human Research activities until you have the final IRB approval letter and the IRB-stamped informed consent form (if applicable) in your possession.
- 2) Personally conduct or supervise the Human Research.
 - a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB, IRB policies, institutional policies, and applicable federal, state and local regulations regarding human subject protection. Relevant institutional and IRB policies and links to federal regulations are located on the HRPP website under IRB Policies and Guidance - <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/policies-and-guidance> . A detailed list of the investigator’s responsibilities is outlined in the “Investigator Responsibilities” policy.
 - b) For clinical trials, conduct the Human Research in accordance with International Conference on Harmonisation (ICH) E6 Good Clinical Practice Consolidated Guidance.
 - c) When required by the IRB, ensure that consent or permission is obtained in accordance with the relevant current protocol, as approved by the IRB, and documented. The participant must document consent on the IRB-stamped informed consent form. This is not necessary if the IRB has issued a waiver of documentation of consent or has waived consent entirely.
 - d) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
 - e) Supervise all study support staff and ensure they are adequately trained for their roles and delegated responsibilities.
 - f) Protect the rights, safety, and welfare of subjects involved in the research.
- 3) Submit to the IRB:
 - a) Proposed modifications as described in this manual. (See “How do I submit a modification?”)
 - b) A continuing review application as requested in the approval letter. (See “How do I submit continuing review?” If your Human Research was determined exempt by the IRB office, you are not required to submit a request for continuing review.

- c) A study completion notice when the Human Research is closed. (See “How Do I Close Out a Study?”) If your Human Research was determined exempt by the IRB office, you are not required to submit a study completion notice.
- 4) Report any new information items on the “Reportable New Information” form to the IRB within five business days. Examples of “new information” are listed on the “Reportable New Information” xform. REMINDER: If the new information requires a modification to the protocol, informed consent or other documents, a “Modification of Approved Human Research” form will need to be submitted to the IRB. See the question “How do I submit a modification?”.
- 5) Disclose any potential financial conflicts of interest for studies submitted to the IRB by having the affected study personnel update their conflict of interest disclosures in COI-Smart.
- 6) Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees.”)
- 7) Do not accept payments designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments”).
- 8) Maintain study documentation and signed and dated consent documents for at least three years after completion of the research and for at least 10 years if the study is conducted at Spectrum Health. Maintain signed and dated HIPAA authorizations and consent documents that include HIPAA authorizations for at least six years after completion of the research.
- 9) When subjects withdraw from FDA-regulated clinical trial follow FDA guidance on data retention: <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126489.pdf>
- 10) For FDA-regulated research involving investigational drugs comply with the following FDA regulations: [21 CFR §312.7](#), [§312.57](#), [§312.59](#), [§312.60](#), [§312.61](#), [§312.64](#), [§312.66](#), [§312.68](#), and [§312.69](#).
- 11) For FDA-regulated research involving investigational devices comply with the following FDA regulations: [21 CFR §812.7](#), [§812.100](#) and [§812.110](#), [§812.145](#), and [§812.150](#).
- 12) For research involving clinical trials, comply with the International Council on Harmonization Efficacy Guidelines: <http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html> (E6(R1) Good Clinical Practice)
- 13) If the Human Research is funded by the Department of Defense (DOD) follow the additional requirements. (See “Are there additional requirements for Department of Defense (DOD) research?”)

How do I conduct the informed consent process?

The online Collaborative Institutional Training Initiative (CITI) human subject protections training program has a module on informed consent which describes the process of obtaining informed consent. The process of obtaining informed consent follows the basic ethical principle of The Belmont Report respect for persons and the federal regulations. The module outlines three main steps for obtaining informed consent: 1) providing information 2) ensuring understanding and 3) obtaining voluntary agreement to participate. For questions or additional training on obtaining informed consent, contact the IRB office at irbassist@spectrumhealth.org or at (616) 486-2031.

How do I document consent?

Use the signature block approved by the IRB. Complete all items in the signature block, including dates and applicable checkboxes.

The following are the documentation requirements for long form (traditional) consent documents:

- The subject, legally authorized representative in the case of adults with diminished decision making capacity, or parent/guardian in the case of minors, prints their name and signs and dates the consent document.
- The individual obtaining consent prints their name and signs and dates the consent document.

- For a subject, legally authorized representative, or parent/guardian in the case of minors, whom are unable to read the consent due to visual impairments or illiteracy/limited English proficiency, and/or whenever required by the IRB or the sponsor, a witness must be present to the entire oral presentation and prints their name and signs and dates the consent document attesting to witnessing the entire consent process. The witness should be provided a copy of the informed consent document to follow along during the process to ensure what was verbally relayed is accurate.
- A copy of the signed and dated consent document is to be provided to the subject, legally authorized representative or parent/guardian in the case of minors, and for Spectrum Health patients a copy is placed in the medical record. The original signed and dated consent document is maintained with other study/regulatory documents.

The following are the documentation requirements for short form consent documents (typically used for non-English speaking subjects when a fully-translated consent is not available):

- *You must obtain IRB approval to use the short form consent for your proposed research study.*
- The subject, legally authorized representative, or parent/guardian in the case of minors, prints their name signs and dates the short form consent.
- The individual obtaining consent signs and dates the IRB approved written summary (English version long form consent).
- The witness to the oral presentation (and interpretation), prints their name and signs and dates the short form consent document **AND** the IRB approved written summary (English version long form consent). The witness should be provided a copy of the IRB approved written summary (English version long form consent) **AND** short form to follow along during the process to ensure what was verbally relayed is accurate.
- A copy of the signed and dated short form consent **AND** signed and dated IRB approved written summary (English version long form consent) is to be provided to the subject, legally authorized representative or parent/guardian in the case in minors, and for Spectrum Health patients a copy is placed in the medical record. The original signed and dated short form consent **AND** signed and dated IRB approved written summary (English version long form consent) is maintained with the other study/regulatory documents.

When Spectrum Health patients are approached for considering participation in a research study and the informed consent process is performed, an entry is required in the patient's medical record recording if the patient declined or consented. If the patient consented, provide a summary of the details surrounding the informed consent discussion in the patient's medical record.

Spectrum Health requires only certified interpreters be used to facilitate the informed consent process and serve as the witness to the oral presentation (and interpretation) when using a short form consent document.

How do I submit a modification?

All modifications/protocol amendments are submitted to the IRB electronically via a secure website designed by IRB Manager. The website address is <https://spectrumhealth.my.irbmanager.com>. You can also access the website via our IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> or by entering the key word "IRB Manager" into any search engine (i.e. Google).

Once logged into the website with your username and password (remember the client name is "spectrumhealth" as one word), enter the study IRB number, complete the "Modification of Approved

Human Research,” located under Start xForm on the left side of the study protocol screen on the IRB Manager website, attach all requested supplements, have the form electronically signed and dated by the investigator, and submit. Maintain paper and electronic copies of all revised documents submitted to the IRB in case further revisions are required. Please note that *research must continue to be conducted without inclusion of the modification until IRB approval of the modification is received* unless the modification is to eliminate an apparent immediate hazard to the subject.

For informed consent document modifications, please submit a track changes (or highlighted changes) copy of the previously approved consent form so changes are easily identified. In addition, submit a clean copy of the revised document as well. Remember the version date of the consent document should be changed when any modifications are made.

If you have already submitted your continuing review and now need to submit a modification, please contact the IRB office at (616) 486-2031 or send an email to irb@spectrumhealth.org and someone will coordinate/link your submissions.

How do I submit continuing review?

All continuing review request are submitted to the IRB electronically via a secure website designed by IRB Manager. The website address is <https://spectrumhealth.my.irbmanager.com>. You can also access the website via our IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> or by entering the key word “IRB Manager” into any search engine (i.e. Google).

Once logged in on the website with your username and password (remember the client name is “spectrumhealth” as one word), enter the study IRB number, complete the “Continuing Review Progress Report”, located under Start xForm on the left side of the study protocol screen on the IRB Manager website, attach all requested supplements, have the form electronically signed and dated by the investigator, and submit.

As a courtesy, the IRB office will issue a reminder email of your upcoming expiration. However, you are ultimately responsible for ensuring your IRB approval does not expire.

If the continuing review involves modifications to previously approved research, submit those modifications as a separate request for modification using the “Modification of Approved Human Research” form as instructed in the above question “How do I submit a modification?”.

If you have already submitted your continuing review and now need to submit a modification, please contact the IRB office at (616) 486-2031 or send an email to irb@spectrumhealth.org and someone will coordinate/link your submissions.

If the approval of Human Research expires (lapses), all Human Research procedures related to the protocol must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection of private identifiable information. Continuing Human Research procedures with an expired IRB approval is a violation of federal regulations. If current subjects will be harmed by stopping Human Research procedures that are available outside the context of Human Research, provide these procedures on a clinical basis, as needed, to protect current subjects from harm. If current subjects will be harmed by stopping Human Research related procedures that are not available outside the Human

Research context, immediately contact the IRB chair at (616) 486-2031 and provide a written list of the currently enrolled subjects and why they will be harmed by stopping Human Research procedures.

If your study IRB approval expires, you will be restricted from submitting any new Human Research for IRB review until a completed application for continuing review or a study completion notice has been received for the study.

*If you are submitting a continuing review for a Humanitarian Use Device (HUD) that is being used consistently with FDA approved labeling for medical treatment (not being studied in the context of a research study for safety and effectiveness) then be sure to select “yes” to the question “Are you seeking continuing approval for a Humanitarian Use Device (HUD) used for medical treatment?” in the “Continuing Review Progress Report” form.

How do I submit unanticipated problems?

All unanticipated problem reports are submitted to the IRB electronically via a secure website designed by IRB Manager. The website address is <https://spectrumhealth.my.irbmanager.com/>. You can also access the website via our IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> or by entering the key word “IRB Manager” into any search engine (i.e. Google).

Once logged into the website with your username and password (remember the client name is “spectrumhealth” as one word), enter the study IRB number, complete the “Reportable New Information” form, located under Start xForm on the left side of the study protocol screen on the IRB Manager website, have the form electronically signed and dated by the investigator, and submit.

Unanticipated problems are to be reported to the IRB **no later than 5 business days** from when you become aware of the information. The “Reportable New Information” form provides guidance on which items and events are reportable to the IRB. REMINDER: If the new information requires a modification to the protocol, informed consent or other documents, a “Modification of Approved Human Research” form will need to be submitted to the IRB. See the question “How do I submit a modification?”.

You will receive an email acknowledging receipt by the IRB office of the unanticipated problem form. Depending on the severity of the unanticipated problem, further actions may be required by the IRB chair or IRB. You will receive a formal letter if further actions are required (i.e. suspending new enrollment).

How do I close out a study?

All study completion notices are submitted to the IRB electronically via a secure website designed by IRB Manager. The website address is <https://spectrumhealth.my.irbmanager.com/>. You can also access the website via our IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/electronic-submission> or by entering the key word “IRB Manager” into any search engine (i.e. Google).

Once logged into the website with your username and password (remember the client name is “spectrumhealth” as one word), enter the study IRB number, complete the “Study Completion Notice” form, located under Start xForm on the left side of the study protocol screen on the IRB Manager website, attach all requested supplements, have the form electronically signed and dated by the investigator and submit.

You will receive a formal letter acknowledging your request to close out the study with the IRB, and you will no longer receive reminder notices or be required to submit further “Continuing Review Progress Reports”.

How long do I keep records?

Maintain your Human Research records, including signed and dated consent documents, for at least three years if not conducted at Spectrum Health and for at least 10 years if the study is conducted at Spectrum Health, after completion of the research. Maintain HIPAA authorizations and other records related to HIPAA compliance for at least six years.

If your Human Research is sponsored, contact the sponsor before disposing of any Human Research records.

What if I need to use an unapproved drug or device in a life-threatening situation and there is no time for prior IRB review?

Contact the IRB office or IRB chair immediately at (616) 486-2031 to discuss the situation. If there is no time to make this contact, see the “WORKSHEET: Emergency Use of a Test Article” for the regulatory criteria allowing such a use and make sure these are followed. This worksheet is located under the “IRB Members” tab on the HRPP website and is the same worksheet the IRB members use to evaluate if the criteria were met. You will need to submit a report of the use to the IRB within five days of the use and an IRB application for initial review within 30 days if there is the possibility of subsequent use of the investigational product.

If you fail to submit the report within five days or the IRB application for initial review within 30 days if there is the possibility of subsequent use of the investigational product, you will be restricted from submitting new Human Research until the report and IRB application for initial review have been received.

Emergency use of an unapproved drug or device in a life-threatening situation without prior IRB review is “research” as defined by FDA, the individual getting the test article is a “subject” as defined by FDA, and therefore the use is governed by FDA regulations for IRB review and informed consent.

Individuals getting an unapproved drug or device in a life-threatening situation without prior IRB review cannot be considered a “subject” as defined by DHHS and their results cannot be included in prospective “research” as that term is defined by DHHS.

Are there additional requirements for Department of Defense (DOD) research?

Yes, when appropriate, research protocols must be reviewed and approved by the IRB prior to DOD approval. Consult with the DOD funding component to see whether this is a requirement. DOD employees (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and check with their supervisor prior accepting such payments. DOD components might have stricter requirements for research-related injury than the DHHS regulations. There also may be specific DOD educational requirements and certifications required. Be sure to indicate on your initial IRB application if your research is receiving DOD funding in order for the IRB to ensure additional requirements by the DOD are met during review.

Does the IRB conduct audits?

Yes, the IRB conducts either for cause or routine audits of investigator consent documents, study conduct, and study documentation. If the IRB or IRB chair has information (i.e. a subject complaint) that the study is

potentially not being conducted in accordance with IRB requirements for protecting research subjects, an inquiry or audit may take place to see if the allegations are founded.

Furthermore, as indicated in the federal regulations 45 CFR §46.109(e) and 21 CFR §56.109(f), the IRB has the authority to observe or have a third party observe the consent process and research.

If the IRB requests to audit your records or observe your consenting practices, you will receive a written notice with further instructions on how to prepare for the audit or observation. At the conclusion of the audit or observation, you will receive a written documentation of any findings, requirements or recommendations.

Do I submit case reports for review?

Case reports generally involve the collection and presentation of detailed information about a particular patient to highlight an interesting condition, treatment, presentation or outcome. There is no intent to test a hypothesis via systematic analysis, analyze data or add to generalizable knowledge. Thus, a case report that documents the clinically indicated care of a single patient does not generally meet the regulatory definition of research. The IRB is responsible for oversight of research activities. A case report that does not meet the definition of research is not subject to IRB oversight and should not be submitted.

- Do not submit case reports involving the collection and presentation of detailed information about a particular patient to highlight an interesting condition, treatment, presentation or outcome.
- Submit for IRB review case reports that may constitute research involving human subjects:
 - Case reports involving three or more patients should be submitted.
 - Case reports incorporating systematic data analysis should be submitted.
 - Case reports testing a hypothesis should be submitted (e.g. treatment A is better than treatment B for this rare condition).
 - See the question, “How do I submit an initial IRB application?”.

For additional information, reference the IRB Guidance Document on Case Reports. This can be found on the HRPP website <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program/policies-and-guidance> .

How do I get additional information and answers to questions?

This document and the policies, forms, and procedures for the Human Research Protection Program are available on the IRB website at <http://www.spectrumhealth.org/research-and-clinical-trials/how-we-can-help/who-we-are/human-research-protection-program> . If you have any questions or concerns about the Human Research Protection Program, contact the IRB office at:

- Phone: (616) 486-2031
- Email: irbassist@spectrumhealth.org

If you have questions, concerns, complaints, allegations of coercion or undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program that cannot be addressed by contacting the IRB office, please contact the Spectrum Health compliance hotline at 1-877-319-0266. The hotline is staffed by an independent organization.