



AAHRPP®

Association for the Accreditation of
Human Research Protection Programs, Inc.®

Guide for Research Sites Seeking Accreditation

(For research sites that only conduct research and do not have their own IRBs)

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Purpose of the Guide

The accreditation process for most research sites is more straightforward than for complex research organizations because most sites only conduct research and the research is regulated by the Food and Drug Administration (FDA).

The first step in the self-assessment is to determine how you will handle the IRB domain. Almost all sites use independent IRBs that are selected by the sponsor or clinical research organization (CRO). So, the first decision you have to make is whether to establish a policy of using only AAHRPP-accredited IRBs. If you decide to use only accredited IRBs, then you complete only Domains I and III of the accreditation standards. The Guide is based on you making that decision.

This Guide includes language that can be inserted into your site's standard operating procedures (SOPs). The language may be modified as long as it meets the regulatory requirements and AAHRPP Standards. The term "reviewing IRB" is used to refer to the independent IRB responsible for a particular study.

Domain I: Organization

Standard I-1: The Organization has a systematic and comprehensive Human Research Protection Program with appropriate leadership.

Element I.1.A. The Organization has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.

If your site only conducts clinical trials and no other types of research, you do not need to include a definition of "clinical investigation" and "human subject" in your SOPs. You must state, however, which regulations or guidelines you follow, such as FDA regulations, ICH-GCP (E6), or ICH-GCP (E6) as adopted by FDA.

If your site conducts clinical trials and other types of research, add to your SOPs the regulations that your site follows for protecting research participants. Include the following definitions of "clinical investigation" and "human subject" as applicable to types of research conducted by your site:

FDA Regulations

Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c))

Human Subject: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.

If your site conducts receives federal funds for conducting research that is not regulated by the FDA, include the following definitions of research

	<p>and human subject.</p> <p>If your site receives funding from a federal agency, such as the Department of Health and Human Services, include the definition of “research” and “human subject.”</p> <p>DHHS Regulations</p> <p><u>Research</u>: A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.</p> <p><u>Human Subject</u>: A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with an individual or identifiable private information.</p> <p>Interaction includes communication or interpersonal contact between an investigator or his or her research staff and the research participant or their private identifiable information.</p> <p>Intervention includes both physical procedures by which data are gathered (e.g.venipuncture) and manipulations of the subjects' environment that are performed for research purposes.</p> <p>Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.</p> <p>If your site conducts studies where it is questionable whether they are regulated by the FDA or another federal agency, add to your SOPs how you decide whether the study is regulated research. Examples of studies where it might be questionable whether they are regulated are:</p> <ul style="list-style-type: none"> • Research using de-identified data sets. • Research on an anonymized tissue samples. • Research on human biomaterials when no identifiers are associated with those materials.
<p>Element I.1.B. The Organization delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program.</p>	<p>Add to your SOPs:</p> <ul style="list-style-type: none"> • The individual (by title) who is responsible for the human research protection program (HRPP) at your research site. This is usually the president, medical director, or partner. • Add this person’s HRPP-related responsibilities, such as: <ul style="list-style-type: none"> ○ Oversees all investigators and members of the research staff (research coordinators). ○ Ensures that investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and all applicable regulations. ○ Ensures there are resources for training, when needed, for investigators and research staff.

Element I.1.C. The Organization has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organizational entities in protecting research participants.

Add to your SOPs:

- (Insert name of research site) must comply with all determinations and requirements of the reviewing IRB for any research conducted at (insert name of research site).
- No individual, including investigators, officials of (insert name of research site), or representatives from a sponsor or CRO may overrule the decisions of the reviewing IRB.

The steps your research site takes to ensure that research involving human participants does not commence until the research has received all approvals.

- Indicate who (by title) reviews and maintains all correspondence from the IRBs to ensure that an approval letter to conduct the study is in the study file.
- State whether a checklist or another method is used to track and maintain the integrity of the study file.
- State whether an individual within (insert name of research site) must grant approval for the study to commence after reviewing correspondence from the IRB.

Develop a SOP, if you don't have one, for reporting undue influence in conducting the study that would compromise the data or harm or reduce protections for research participants:

- To whom (by title) investigators and research staff can report undue influence.
- The individual (by title) who is responsible to investigate any allegation of undue influence and take corrective action.

Undue influence is generally defined as an individual in an authoritative position taking advantage of his or her position of power and using it over another person. Examples of undue influence include:

- An investigator asked by his or her supervisor to falsify study data.
- A member of the research staff being asked by an investigator to falsify accrual numbers for research participants.
- A member of the research staff being asked by an individual in an authoritative position to falsify a consent document that was not appropriately signed by a research participant.

Element I.1.D. The Organization has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to Sponsors, Researchers, Research Staff, research participants, and the Institutional Review Board or Ethics Committee, as appropriate.

State whether you follow the FDA regulations or ICH-GCP (E6) or ICH-GCP (E6) as adopted by FDA.

Include a statement that your (insert name of research site) expects investigators and research staff and the organizational official to comply with the FDA regulations or ICH-GCP (E6) or ICH-GCP (E6) as adopted by FDA and the ethical standards on which they are based.

Include a statement in your SOPs that clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with GCP and the applicable regulatory requirements.

Add to your SOPs a description of the mechanism for communicating or making available the SOPs related to the HRPP. Either mechanism is

	<p>sufficient:</p> <ul style="list-style-type: none"> • SOPs are made available to internal staff (including investigators and members of the research staff) via an internal intranet system. State that SOPs are made available to sponsors and CROs upon request. • Each employee receives a hard copy of the SOPs related to the HRPP. SOPs are made available to sponsors and CROs upon request. <p>State how changes in the SOPs are communicated to all individuals within the HRPP. For instance, when SOPs are revised or new policies are added, individuals within the HRPP are notified by way of any of the following mechanisms:</p> <ul style="list-style-type: none"> • An e-mail is sent out to all internal staff notifying them that an SOP was revised and the updated version is available on the Web site. • Revised SOPs are circulated via the e-mail listserv to all individuals within the HRPP. • Hard copies of revised SOPs are circulated to members of the HRPP. <p>Include an organizational chart that includes all of the components that are involved with human research protection, such as:</p> <ul style="list-style-type: none"> • Investigators and research staff. • Individuals responsible for quality control and assurance. • Individuals responsible for the storage and control of investigational products.
<p>Element I.1.E. The Organization has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants.</p>	<p>List the training activities you provide that contribute to the improvement of the qualifications and expertise of investigators and research staff or others involved in protecting the rights and welfare of research participants. Some examples of training activities are:</p> <ul style="list-style-type: none"> • ICH-GCP (E6) training for investigators and research staff. • CITI training modules for investigators and research staff. • Training curriculum developed by your site for the protection of research participants. • Attendance at national meetings, such as DIA, BIO, ACRP, or SOCRA. <p>You can list more than one of the training activities. A description of activities beyond the examples provided above is encouraged.</p> <p>Add to your SOPs initial training requirements for investigators and research staff and other individuals involved in protecting research participants at your research site. For instance:</p> <ul style="list-style-type: none"> • Investigators and research staff must complete the training prior to participating in any research studies. • Investigators and research staff have to obtain specific certifications prior to conducting research. <p>Add to your SOPs the individual (by title) who ensures that each individual involved in the protection of research participants fulfills the (insert name of your research site) training requirements.</p> <p>Add to your SOPs continuing training requirements. This description must include:</p> <ul style="list-style-type: none"> • The individual (by title) who monitors investigators and research staff to ensure that training requirements are fulfilled.

<p>Element I.1.F. The Organization has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process.</p>	<ul style="list-style-type: none"> • The actions taken when training requirements are not fulfilled. <p>State that (insert name of your research site) relies on the sponsor or the IRB reviewing the research to ensure that it is scientifically valid. State that even though scientific review of research is conducted by the sponsor or the IRB reviewing the research, the investigator will review the protocol prior to beginning the study to ensure that the research will follow procedures consistent with sound research design.</p>
<p>Element I.1.G. The Organization has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws.</p>	<p>Add to your SOPs the regulations relevant to research involving humans as participants, such as:</p> <ul style="list-style-type: none"> • FDA regulations 21 CFR 50, 21 CFR 56, 21 CFR 312, 21 CFR 812, 21 CFR 54, 21 CFR 11. • ICH-GCP (E6) or ICH-GCP (E6) as adopted by FDA, if applicable. • DHHS regulations 45 CFR 46, if you receive federal funding to conduct research. <p>List the state laws that affect the way you conduct research in the state in which your research site(s) is located. If you conduct research with children and cognitively impaired participants, your SOPs must include a definition of the following individuals in accordance with your state's laws:</p> <ul style="list-style-type: none"> • Children. • Guardians. • Legally authorized representatives or surrogates (those individuals who consent to the procedures of research on behalf of another individual). <p>If your site conducts research in more than one state, provide definitions of the above individuals for each state where your site conducts research.</p>
<p>Standard I-2: The Organization ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the Organization conducts or oversees.</p>	
	<p>Add to your SOPs the plan to evaluate resources needed for the HRPP. Include in this description:</p> <ul style="list-style-type: none"> • The individual(s) (by title) responsible for evaluating the resources of the HRPP to ensure that they are adequate to protect research participants. Resources may be as follows: <ul style="list-style-type: none"> ○ Number of qualified staff (ICH-GCP (E6)). ○ Facility space (ICH-GCP (E6)). ○ Equipment for the types of research conducted by the research site. ○ Technological capabilities to store and control data. ○ Space, equipment, and technology to control investigational test articles. ○ Staff to liaison with the sponsor or CRO and the IRB reviewing the research. • Indicate how often this evaluation occurs (e.g., annually). • Indicate the individual (by title) who evaluates resources on a study-by-study basis to ensure that they are adequate to protect research participants. For instance, specify the individual (by title) who determines that the equipment, facility space, and technology needed for each study is adequate.
<p>Standard I-3: The Organization's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent</p>	

levels of participant protection as research conducted in the Organization’s principal location while complying with local laws and taking into account cultural context.

This Standard is not applicable unless you conduct research outside the United States.

Standard I-4: The Organization responds to the concerns of research participants.

Element I.4.A. The Organization has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan.

Add to your SOPs:

(Insert name of your research site) relies on the reviewing IRB to include in consent documents contact information for an individual who is unaffiliated with a specific research study to:

- Discuss problems, concerns, and questions.
- Obtain information.
- Offer input.

Add information to your Web site or create a brochure for prospective participants that provides contact information for an individual (insert the name of individual within your site who does not conduct research, but is familiar with the protection of participants) who is unaffiliated with a specific research study to:

- Discuss problems, concerns, and questions.
- Obtain information.
- Offer input.

Add to your SOPs the steps your research site follows to respond to contacts from participants or others. For example, if a research participant has a question about a study being advertised at your research site, add to your SOPs the process for answering his or her questions. Or, if a participant voices a complaint about an ongoing study in which he or she is a participant, add to your SOPs the steps taken to address the complaint and whether it needs to be reported to the IRB for review.

Element I.4.B. The Organization conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.

Add to your SOPs the methods for enhancing the understanding of current participants, prospective participants, and communities from which you recruit participants into studies. Your SOPs should include:

- A list of training or outreach activities provided to research participants. This includes, but is not limited, to:
 - Brochures that include information about an individual’s rights as a research participant and information about the types of research conducted at your research site.
 - Web site materials that offer information about the clinical research process and provide information to participants about what participation in research entails. Some sites choose to provide information about:
 - The features of the clinical research process in bringing new products to the market.
 - Protections built into the clinical research process such as IRB review and data and safety monitoring.
 - The ongoing consent process.
 - Any conferences, seminars, or open houses that your research site hosts in order to provide the community with information about the types of research conducted by your research site and information

	<p>about rights and interests of research participants.</p> <p>Add to your SOPs how you periodically evaluate outreach materials and activities. This description should address the following points:</p> <ul style="list-style-type: none"> • The frequency with which outreach activities are evaluated (e.g. annually). • The individual (by title) who conducts the evaluation. • That the results of this evaluation are used to make improvements to the existing outreach materials and activities.
<p>Element I.4.C. The Organization promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.</p>	<p>Generally, this Element is not applicable to your research site.</p>
<p>Standard I-5: The Organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program.</p>	
<p>Element I.5.A. The Organization conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization makes improvements to increase compliance, when necessary.</p>	<p>Create a quality improvement plan that periodically assesses the compliance of the HRPP. In the plan:</p> <ul style="list-style-type: none"> • Create a goal statement indicating that the goal of the quality improvement plan is to achieve and maintain compliance with the SOPs of the HRPP and all regulations governing the conduct of research. • In this plan, define at least one measure of compliance. Examples of measures of compliance are: <ul style="list-style-type: none"> ○ That 100% of consent documents in each study file are signed and dated by a participant or the participant’s legally authorized representative. ○ That an IRB approval letter is included in 100% of the study files for each research study. ○ That 100% of protocol deviations are reported to the reviewing IRB in accordance with the reporting requirements. ○ That 100% of recruitment materials used for each study are included in the study file along with documentation from the reviewing IRB that they were approved. ○ That each investigator has documentation in his or her training file indicating that training was completed as required by (insert name of research site). ○ That 100% of interim or continuing review reports required by the reviewing IRB are submitted in accordance with the deadlines specified in the IRB approval letter. • Add to your SOPs the frequency with which the given measures of compliance are assessed (e.g. annually). • Add to your SOPs the individual (by title) who assesses the data and directs improvements to the HRPP to ensure that any identified compliance deficiencies are rectified.
<p>Element I.5.B. The Organization conducts audits or surveys or uses other methods to assess the</p>	<p>Create a quality improvement plan that periodically assesses the quality, efficiency, and effectiveness of the HRPP. In the plan:</p>

<p>quality, efficiency, and effectiveness of the Human Research Protection Program. The Organization identifies strengths and weaknesses of the Human Research Protection Program and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the program.</p>	<ul style="list-style-type: none"> • Create a goal statement indicating that the goal of the quality improvement plan is to improve the quality, efficiency, and effectiveness of the HRPP. • In this plan, define at least one measure of quality, efficiency, and effectiveness of the HRPP. Examples of such measures are: <ul style="list-style-type: none"> ○ Turn-around-time from IRB submission to approval. ○ Time from IRB approval to enrollment of allotted number of research participants. ○ Average time to respond to a question, concern, or complaint from a research participant. ○ Average time from identifying an adverse event to reporting the event to the sponsor or CRO. • State the frequency with which the given measures of quality, efficiency, and effectiveness are assessed (e.g. annually). <p>Add to your SOPs the individual (by title) who assesses the data and directs improvements to the HRPP in order to promote greater quality, efficiency, and effectiveness in the measured process improves.</p>
<p>Element I.5.C. The Organization has and follows written policies and procedures so that Researchers and Research Staff may bring forward to the Organization concerns or suggestions regarding the Human Research Protection Program, including the ethics review process.</p>	<p>Inform investigators and research staff how to obtain answers to questions, express concerns, and convey suggestions regarding your HRPP. You can do this in any of the following ways:</p> <ul style="list-style-type: none"> • Add a section to your Web site that provides investigators and research staff with information about whom they can contact to obtain answers to questions, express concerns, and convey suggestions regarding your HRPP. • Add this information to your SOPs. • Create a flyer that is distributed to investigators and members of the research that informs them about who they can contact to obtain answers to questions, express concerns, and convey suggestions regarding your HRPP.
<p>Element I.5.D. The Organization has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. The Organization works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when noncompliance occurs. Such policies and procedures include reporting these actions, when appropriate.</p>	<p>Create a SOP or ensure that your current SOP on non-compliance includes:</p> <p>(Insert the name of your research site) has a process for identifying non-compliance and reporting each instance of non-compliance to the reviewing IRB in accordance with its SOPs.</p> <p>Indicate whether your research site is required to report non-compliance to the sponsor or CRO in addition to reporting to the reviewing IRB.</p> <p>Add the following definition of non-compliance to your SOPs: Non-compliance is a failure to follow the regulations or the requirements and determinations of the reviewing IRB. Provide some examples of events that constitute non-compliance, such as:</p> <ul style="list-style-type: none"> ○ Participant complaints indicating that a member of the research staff jeopardized the participant’s rights and welfare. ○ A failure of an investigator or a member of the research staff to obtain consent. ○ A failure of an investigator or member of the research staff to administer an investigational product in accordance with the protocol.

	<ul style="list-style-type: none"> ○ A failure of a member of the research staff to maintain the confidentiality of participants' research-related data. ○ Protocol deviations. ○ Any event that is discovered during a sponsor or CRO audit that meets the definition of non-compliance. <p>Add to your SOPs:</p> <ul style="list-style-type: none"> ● The individuals who are responsible for identifying non-compliance (at a minimum, this should include investigators and members of the research staff and any individuals responsible for research oversight). ● The individual (by title) who is responsible for reporting non-compliance to the IRB. ● Investigators and research staff must comply with the corrective actions resulting from the IRBs' review of non-compliance. ● Any non-compliance determined to be serious or continuing in nature must be reported to officials of your organization and FDA (for FDA-regulated research). <p>Note: If your research site relies on the reviewing IRB to report serious or continuing non-compliance to FDA, then state that (insert the name of your research site) relies on the reviewing IRB to report serious or continuing non-compliance to FDA.</p>
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Standard I-6: The Organization has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated.

<p>Element I.6.A. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the Organization that could influence the conduct of the research or the integrity of the Human Research Protection Program.</p>	<p>This Element is not applicable to your research site. If your site receives gifts for research, has investments, or holds patents, contact AAHRPP for advice in addressing this Element.</p>
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<p>Element I.6.B. The Organization has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and Research Staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. The Organization works with the IRB in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.</p>	<p>Add to your SOPs that the following must be disclosed as financial conflicts of interest by investigators and members of the research staff:</p> <p>FDA Requirements:</p> <ul style="list-style-type: none"> ● Ownership interest, stock options, or other financial interest related to the research unless it meets two tests: <ul style="list-style-type: none"> ○ Does not exceed \$50,000 when aggregated for the immediate family. ○ Publicly traded on a stock exchange. ● Compensation related to the research unless it: <ul style="list-style-type: none"> ○ Does not exceed \$25,000 in the past year when aggregated for the immediate family. ● Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement. <p>Indicate in your SOPs that the financial interest investigators and research staff must disclose include those of their immediate family members. Define immediate family members as spouse and dependent children.</p> <p>Add to your SOPs a description of the process for investigators and</p>
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members of the research staff to disclose financial conflicts of interest. This description should include:

- To whom investigators and research staff are required to disclose conflicts of interest.
 - To the IRB reviewing the research.
 - To an individual, department, or committee within your research site responsible for reviewing conflicts of interest prior to submission to the IRB.
 - To both of the above entities.
- How conflicts of interest are disclosed by investigators and members of the research staff (e.g., financial disclosure form).
 - Using the financial disclosure form of the reviewing IRB.
 - Using an internal financial disclosure form.
- The frequency by which investigators and research staff are required to disclose conflicts of interest.
 - On a study-by-study basis to the IRB.
 - Annually to (title of person or name of entity) within the HRPP.

Add to your SOPs the process for reviewing disclosed financial interests, such as:

- Whether your research site relies on the reviewing IRB to review any financial interests disclosed as part of the research submission process.
- Whether your research site reduces or eliminates financial interest of investigators and research staff below the reporting threshold required by the IRB prior to study submission.

If your research site relies on the reviewing IRB to review and manage significant financial interests (conflicts of interest), state in your SOPs that all investigators and members of the research staff must comply with the plans for managing conflicts of interest as required by the reviewing IRB.

If you conduct some research that is also sponsored in by DHHS, then the PHS disclosure standards must be applied to all research.

PHS Requirements:

- Ownership interest, stock options, or other financial interest related to the research unless it meets four tests:
 - Does not exceed \$10,000 when aggregated for the immediate family.
 - Publicly traded on a stock exchange.
 - No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research.
 - Does not exceed 5% interest in any one single entity when aggregated for the immediate family.
- Compensation related to the research unless it meets two tests:
 - Does not exceed \$10,000 in the past year when aggregated for the immediate family.
 - No arrangement has been entered into where the amount of compensation will be affected by the outcome of the research. [e.g., an arrangement has been made where the value of the interest will

	<p>change depending on the outcome of the research.]</p> <ul style="list-style-type: none"> Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
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Standard I-7: The Organization has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.

<p>Element I.7.A. When research involves investigational or unlicensed test articles, the Organization confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.</p>	<p>Add to your SOPs:</p> <ul style="list-style-type: none"> The process to obtain approvals from the FDA. (Applies only when your research site or one of your investigators is in the role of sponsor and must obtain an IND or IDE number for a given study). That when conducting an FDA-regulated study that involves a drug or device with an IND or IDE number, that (insert position or title, e.g., investigator) confirms that the IND or IDE number provided in the sponsor’s protocol is valid. That the investigator must record the IND or IDE number on the submission form that is submitted to the reviewing IRB. <p>Indicate that if a study involves an FDA-regulated product, but no IND or IDE number is provided by the sponsor, indicate who (by title) confirms that the research meets one of the following IND or IDE exemptions:</p> <p>IND Exemptions</p> <p>Exemption 1</p> <ul style="list-style-type: none"> The drug product is lawfully marketed in the United States. (Investigator confirms with sponsor) The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.(Investigator confirms with sponsor) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product. (Investigator confirms with sponsor). The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.(Investigator confirms with sponsor) The investigation is conducted in compliance with 21 CFR 50 and 56.(IRB confirms) The investigation is conducted in compliance with the requirements of 21 CFR 312.7.(Investigator confirms with sponsor) <p>Exemption 2</p> <ul style="list-style-type: none"> A clinical investigation is for an in vitro diagnostic biological product that involves one or more of the following: (Investigator confirms with sponsor) <ul style="list-style-type: none"> Blood grouping serum. Reagent red blood cells. Anti-human globulin.
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	<ul style="list-style-type: none"> • The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure.(Investigator confirms with sponsor) • The diagnostic test is shipped in compliance with 21 CFR 312.160. <p>Exemption 4</p> <ul style="list-style-type: none"> • A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND. <p>IDE Exemptions</p> <ul style="list-style-type: none"> • A diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing: <ul style="list-style-type: none"> ○ Is noninvasive. (Investigator confirms) ○ Does not require an invasive sampling procedure that presents significant risk. (IRB confirms) ○ Does not by design or intention introduce energy into a participant. (Investigator confirms) • Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure. • A device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put participants at risk. (Investigator confirms) • A custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution. <p>Indicate that if the sponsor determines that a device involves non-significant risk and does not include an IDE number that the investigator will ensure that the research will be conducted in accordance with the following abbreviated IDE requirements:</p> <ul style="list-style-type: none"> • Consent will be obtained from each subject under the investigator’s care in accordance 21 CFR 50 and documents the consent accordingly, unless documentation is waived.
<p>Element I.7.B. The Organization has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements.</p>	<p>Add to your SOPs the process to control investigational drugs and devices so that they are used only in approved research protocols and under the direction of approved investigators. Add:</p> <ul style="list-style-type: none"> • That storage and control of investigational products includes: <ul style="list-style-type: none"> ○ Receipt of investigational products. ○ Labeling of investigational products. ○ Distribution of investigational products. ○ Accounting for investigational products. ○ Destruction of investigational products. • The processes for the receiving investigational products. These should include: <ul style="list-style-type: none"> ○ The individual (by title) who reviews the shipping instructions of the product to ensure that they were followed. ○ The individual (by title) who is responsible for documenting receipt

of the investigational product and including this documentation in the file.

- The individual (by title) who is responsible for ensuring that the appropriate amount of study product was sent and that the shipment invoice corresponds to the received products. Indicate how this information is documented.
- The individual (by title) who is responsible for identifying product defects and communicating this information back to the sponsor. Indicate where this information is documented.
- The processes for labeling investigational products. These should include who verifies the following:
 - The name and identification number of the product is present on the label.
 - The label includes the expiration date of the product.
 - The recommended storage conditions for the product are included on the label.
 - The lot number of the product is included on the label.
 - The name and address of the sponsor is included on the label.
 - The code or protocol identification number is included on the label.
- The processes for storing investigational products. These should include:
 - The investigational product must be stored in a locked location.
 - The temperature in which investigational products are stored should be consistent with the products' labeling.
 - The individual (by title) who is responsible for performing these procedures.
- The processes for distributing investigational products. These should include:
 - The investigator or a member of the study staff designated by the investigator must inform the participant about the proper use of the investigational product.
 - The individual (by title) who ensures on a continual basis that the product is being used in accordance with the protocol.
 - The individual (by title) who records any deviations in the proper use of the investigational product and submits such deviations to the reviewing IRB.
 - The individual (by title) who informs participants that they are responsible for returning all unused investigational product and its packaging (e.g., bottle, syringe, container) to the research team.
- The processes for accounting for investigational products. These should include:
 - The individual (by title) who is responsible for documenting the quantity of the investigational product used for each participant.
 - The individual (by title) who is responsible for comparing the amount of investigational product returned from a participant against the amount used and documents any inconsistencies.
 - A statement that under no circumstances may an investigational product be distributed to an individual not participating in the study or another research site.
 - The individual (by title) who retains accountability logs for each

	<p>study and how long these logs must be maintained.</p> <ul style="list-style-type: none"> • The processes for destroying investigational products. These should include: <ul style="list-style-type: none"> ○ The individual (by title) who is responsible for returning any unused investigational products to the research sponsor. ○ If investigational products will not be returned, the individual (by title) who is responsible for ensuring that products are appropriately destroyed. ○ Destroying unused investigational products. • The length of time that documentation is maintained for each of the above procedures. <p>Include as part of the above SOPs:</p> <ul style="list-style-type: none"> • Where allowed or required, the investigator may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator. • The investigator, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants. Investigators should maintain records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.
<p>Element I.7.C. The Organization has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article.</p>	<p>Generally, this Element is not applicable to research sites.</p>
<p>Standard I-8: The Organization works with public, industry, and private Sponsors to apply the requirements of the Human Research Protection Program to all participants.</p>	
<p>Element I.8.A. The Organization has a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.</p>	<p>Submit either a template contract or a checklist used to negotiate contracts with research sponsors which states that contracts must define the party (e.g., research site or sponsor) that is responsible to pay for care when a participant suffers a research-related injury.</p>
<p>Element I.8.B. In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the Organization has a written agreement with the Sponsor that the Sponsor promptly reports to the Organization findings that could affect the safety of participants or influence the conduct of the study.</p>	<p>Submit either a template contract or a checklist used to negotiate contracts with research sponsors which states that contracts must obligate the sponsor to promptly report to (insert the name of the individual (by title) or department within your research site) any findings that could:</p> <ul style="list-style-type: none"> • Affect the safety of participants. • Influence the conduct of the study.

<p>Element I.8.C. When the Sponsor has the responsibility to conduct data and safety monitoring, the Organization has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the Organization.</p>	<p>Submit either a template contract or a checklist used to negotiate contracts with research sponsors which states that contracts must obligate the sponsor to send data and safety monitoring plans and reports to (insert the name of the individual (by title) or department your research site) within (specify the timeframe). The template contract or checklist must also have contracts obligate the sponsor to provide urgent data and safety monitoring reports to (insert the name of your research site) within (insert timeframe).</p>
<p>Element I.8.D. Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.</p>	<p>Generally, this Element only applies to your research site if you have a publication policy.</p>
<p>Element I.8.E. When participant safety could be directly affected by study results after the study has ended, the Organization has a written agreement with the Sponsor that the Researcher or Organization will be notified of the results in order to consider informing participants.</p>	<p>Submit either a template contract or a checklist used to negotiate contracts with research sponsors which states that contracts must obligate the sponsor to communicate findings from a closed research study to (insert the name of your research site) when those findings could directly affect the safety of past participants. The template contract or checklist must also specify a timeframe after closure of the study during which the sponsor will communicate such findings (e.g., as appropriate to the type of study such as two years or indefinitely).</p>

Domain III: Researcher and Research Staff

Standard III-1: In addition to following applicable laws and regulations, Researchers and Research Staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, Researchers and Staff have the protection of the rights and welfare of research participants as a primary concern.

<p>Element III.1.A. Researchers and Research Staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate.</p>	<p>Your SOPs in support of Element I.1.A also address this Element. Also submit materials that inform investigators and members of the research staff on the kinds of activities that require IRB review and approval. Such materials include information published on your Web site, investigator training materials, or an investigator handbook.</p>
<p>Element III.1.B. Researchers and Research Staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with the Organization, manage, minimize, or eliminate financial conflicts of interest.</p>	<p>Your SOPs and disclosure forms, (including FDA Forms 3454 and 3455) in support of Element I.6.B also address this Element. Also submit materials which inform investigators and members of the research staff on the kinds of interests that must be disclosed internally (within your research site) or to the reviewing IRB as conflicts of interest. Such materials include information published on your Web site, investigator training materials, or an investigator handbook.</p>
<p>Element III.1.C. Researchers employ sound study design in accordance with the standards of their discipline. Researchers design studies in a manner that minimizes risks to participants.</p>	<p>Submit materials which inform investigators and members of the research staff about assessing risks and potential benefits in research studies. The content of the training materials should include the regulatory criteria for approval of research related to risks and potential benefits:</p> <ul style="list-style-type: none"> • Risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily

expose participants to risk.

- Risks to participants are minimized, when appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.

Risks to participants are reasonable in relationship to the potential benefits, if any, to participants, and the importance of the knowledge that may be expected to result.

Note: For the above three bullets, indicate that for industry-sponsored research, the investigator relies on the sponsor or the reviewing IRB to ensure that the research satisfies the above criteria. If the investigator is responsible for the design of the study, indicate that he or she must design the study in accordance with the above criteria.

Add to your SOPs that the investigator must ensure that all members of the research staff comply with the provisions for monitoring data to ensure the safety of participants to be appropriate, as described in the approved protocol.

Note: Indicate that when the investigator is responsible for the design of research, that he or she must ensure, that, when appropriate, the study includes a plan of monitoring data to ensure the safety of participants.

Add to your SOPs:

- The investigator must communicate to the reviewing IRB on the submission form whether some or all of the participants are likely to be vulnerable to coercion or undue influence.
- Identify the vulnerable populations that you are likely to enroll at your research site given the types of research conducted and the community in which your site is located. Such populations may be as follows:
 - Pregnant women (fetuses and neonates).
 - Children.
 - Economically disadvantaged persons.
 - Individuals who are homeless.
 - Individuals who are illiterate.
 - Cognitively impaired individuals such as those suffering from mental illness or who are cognitively impaired.
 - Individuals who are not fluent in the primary language spoken in your country or in the location of the research site.
- The investigator includes on the submission form any additional safeguards included in the protocol and at the research site to protect their rights and welfare.

Add to your SOPs that the investigator and research staff must implement any additional safeguards required by the reviewing IRB to protect vulnerable populations. For instance, if conducting research with cognitively impaired participants such as individuals suffering from Alzheimer's disease, the investigator must have a mechanism for assessing the person's capacity to give consent prior to seeking consent from a legally authorized representative.

Add to your SOPs and training materials for investigators and research staff:

- A qualified physician (or dentist, when appropriate), who is an

	<p>investigator or a co- investigator for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions.</p> <ul style="list-style-type: none"> • During and following a participant’s participation in a clinical trial, the investigator ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial. • Investigators inform participants when medical care is needed for other illnesses of which the investigators become aware. • The investigator follows the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the investigator promptly documents and explains to the sponsor any premature unblinding.
<p>Element III.1.D. Researchers determine that the resources necessary to protect participants are present before conducting each research study.</p>	<p>Cite the same materials provided in response to the relevant sections of Element III.1.C above.</p>
<p>Element III.1.E. Researchers and Research Staff recruit participants in a fair and equitable manner.</p>	<p>Add to your SOPs and training materials that the investigator must communicate the following to the reviewing IRB in the submission form:</p> <ul style="list-style-type: none"> • The setting in which the research will be conducted. • Whether prospective participants will be vulnerable to coercion or undue influence. • Participant recruitment and enrollment procedures. • The amount and timing of payments to participants. <p>State that no advertisements or recruitment procedures may be used if they are not first reviewed and approved by an IRB.</p> <p>When an investigator or member of the research staff is responsible for creating advertisements, state that advertisements must include:</p> <ul style="list-style-type: none"> • The name and address of the investigator or research facility. • The purpose of the research or the condition under study. • In summary form, the criteria that will be used to determine eligibility for the study. • A brief list of benefits to participants, if any. • The time or other commitment required of the participants. • The location of the research and the person or office to contact for further information. <p>Indicate that advertisements must not:</p> <ul style="list-style-type: none"> • State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. • Include exculpatory language. • Emphasize the payment or the amount to be paid, by such means as larger or bold type. • Promise “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation. • Make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling. • Use terms, such as “new treatment,” “new medication,” or “new drug,” without explaining that the test article is investigational.

	<ul style="list-style-type: none"> • Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing. <p>For payments to research participants, the investigator must ensure that:</p> <ul style="list-style-type: none"> • Credit for payment accrues as the study progresses and is not contingent upon the participant completing the entire study. • All information concerning payment, including the amount and schedule of payments, is set forth in the consent document. <p>State in your SOPs that the following are prohibited your research site or allowed under certain circumstances and describe the circumstances:</p> <ul style="list-style-type: none"> • Payment arrangements in exchange for referrals of prospective participants (“finder’s fees” or “referral fees”) are allowable at your research site. • Payment arrangements designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments”). <p>Add to your SOPs:</p> <ul style="list-style-type: none"> • The investigator informs the participant’s primary physician about the participant’s participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed. • Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the investigator makes a reasonable effort to ascertain the reason, while fully respecting the participant’s rights.
<p>Element III.1.F. Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants.</p>	<p>Add to your SOPs and training materials that the investigator must communicate to the reviewing IRB on the submission form:</p> <ul style="list-style-type: none"> • The person who will conduct the consent discussion. • The person who will provide consent or permission. • Any waiting period between informing the prospective participant and obtaining consent. • Steps taken to minimize the possibility of coercion or undue influence. • The language used by those obtaining consent. • The language understood by the prospective participant or the legally authorized representative. • The information to be communicated to the prospective participant or the legally authorized representative. <p>Add to your SOPs that the investigator must ensure that consent is obtained in accordance with the following requirements:</p> <ul style="list-style-type: none"> • The investigator will obtain the legally effective consent of the participant or the participant’s legally authorized representative. • The circumstances of the consent process provide the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate. • The circumstances of the consent process minimize the possibility of coercion or undue influence. • The individuals communicating information to the participant or the legally authorized representative during the consent process will

provide that information in language understandable to the participant or the representative.

- The information being communicated to the participant or the representative during the consent process will not include exculpatory language through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant's legal rights.
- The information being communicated to the participant or the legally authorized representative during the consent process will not include exculpatory language through which the participant or the legally authorized representative releases or appears to release the investigator, the sponsor, the site, or its agents from liability for negligence.

Documentation of Consent

- The consent document embodies the basic and required additional element of disclosure (Indicate that the reviewing IRB will must ensure that the consent document embodies the basic and required additional elements of disclosure).
- The participant or the participant's legally authorized representative will sign and date the consent document.
- A copy of the signed and dated consent document will be given to the person signing the consent document.
- The investigator will give either the participant or the representative adequate opportunity to read the consent document before it is signed.

If the short form consent process is used, have the investigator ensure that:

- That the consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant's legally authorized representative.
- A written summary embodies the basic and required additional elements of disclosure.
- There will be a witness to the oral presentation.
- For participants who do not speak English, the witness is conversant in both English and the language of the participant.
- The participant or the participant's legally authorized representative will sign the consent document.
- The witness will sign and date both the short form and a copy of the summary.
- The person actually obtaining consent will sign and date a copy of the summary.
- A copy of the signed and dated short form will be given to the participant or the legally authorized representative.
- A copy of the signed and dated summary will be given to the participant or the legally authorized representative.

Research Data Retention

Add to your SOPs:

- When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study

database and may not be removed. The consent document cannot give the participant the option of having data removed.

- The investigator may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant must distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

Note: The investigator must obtain the participant's informed consent for this limited participation in the study using the informed consent form approved by the IRB for these purposes.

- If a participant limited participation in the study (assuming such a situation was not withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

Observation of the Consent Process

Add to your SOPs that the IRB has the authority to observe the consent process as a method to protect participants. State that investigators and members of the research staff conducting research at (insert name of your research site) must allow this observation to take place, as required by the reviewing IRB.

Waiver or Alteration of the Consent Process

Add to your SOPs a statement that the consent process cannot be waived or altered under the FDA regulations.

Add to your SOPs:

- The requirement to document the consent process may be waived only when the following criteria are met:
 - The research presents no more than minimal risk of harm to participants.
 - The research involves no procedures for which written document of the consent process is normally required outside of the research context.

Indicate that documentation of consent may be waived only when the reviewing IRB makes this determination. In cases in which documentation of the consent process is waived, the IRB may require the investigator to provide participants with additional information about the research.

Add to your SOPs and training materials for investigators and research staff: Investigators and research staff provide all the disclosures and

	follow the requirements pertaining to consent covered by ICH-GCP (E6).
Element III.1.G. Researchers and Research Staff have a process to address participants' concerns, complaints, or requests for information.	Your SOPs in support of Element I.4.A. address this Element.
Standard III-2: Researchers and Research Staff meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the Organization's policies and procedures for protecting research participants; and the IRB's or EC's determinations.	
Element III.2.A. Researchers and Research Staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the Organization's policies and procedures regarding the protection of research participants.	<p>Your SOPs in Element I.1.D address this Element. Also submit materials that inform investigators and research staff of their ethical obligations in conducting research involving human participants. Such materials include information published on your Web site, investigator training materials, or an investigator handbook.</p> <p>Include in your SOP and training materials:</p> <ul style="list-style-type: none"> • The investigator provides evidence of his or her qualifications through an up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority. • The investigator is familiar with the appropriate use of the investigational product in the current investigator brochure, in the product information, and in other information sources provided by the sponsor. • The investigator permits monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority. • The investigator ensures the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor. • The investigator maintains the clinical trial documents as specified in Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. • Essential documents are retained until at least two years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational product.
Element III.2.B. Researchers maintain appropriate oversight of each research study, as well as Research Staff and trainees, and appropriately delegate research responsibilities and functions.	<p>Include in your SOPs and training materials for investigators and members of the research staff:</p> <ul style="list-style-type: none"> • The investigator must maintain a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties.
Element III.2.C. Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the Organization and to the requirements or determinations of the IRB.	Your SOPs in support of Element I.5.D address this Element. Also submit materials that inform investigators on the kinds of events that require reporting to the reviewing IRB as cases of non-compliance. Such materials include information published on your Web site, investigator training materials, or an investigator handbook.
Element III.2.D. Researchers and Research Staff follow reporting requirements in accordance with	Your SOPs in support of Element I.5.D also address this Element. Also submit materials that inform investigators about the kinds of events that

applicable laws, regulations, codes, and guidance; the Organization's policies and procedures; and the IRB's or EC's requirements.

require reporting to the reviewing IRB as allegations of non-compliance. Such materials include information published on your Web site, investigator training materials, or an investigator handbook.

State that investigators must report all adverse events, serious adverse events to the sponsor or CRO in accordance with the sponsor or CROs' reporting requirements.

State that investigators must report unanticipated problems involving risks to participants or others to the reviewing IRB in accordance with their reporting requirements.

Unanticipated problems involving risks to participants or others are defined as any event that meets all of the following criteria:

- Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are Add to your SOPs in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Is 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
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

List the following types of events that should always be reported to the reviewing IRB as an unanticipated problem involving risks to participants or others:

- Information that indicates a change to the risks or potential benefits of the research. For example:
 - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
 - A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to the IRB.
- A breach of confidentiality.
- Change in the labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
- Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
- Incarceration of a participant in a protocol not approved to enroll prisoners.
- Event that requires prompt reporting to the sponsor.
- Sponsor imposed suspension for risk.
- Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.

Indicate that unanticipated problems involving risks to participants or others may be clinical or non-clinical in nature.

Indicate the individual (by title) who is responsible for reporting adverse events, serious adverse events, and unanticipated problems involving risks to participants or others to the sponsor, CRO, and reviewing IRB, as applicable.

Note: Adverse events and serious adverse events are not unanticipated problems involving risks to participants or others when they are expected or foreseeable or the level of risk associated with the event is what was previously known and approved by the IRB.

Add to your SOPs that IRBs have the authority to suspend or terminate the approval of research that:

- Is not being conducted in accordance with the IRB's requirements.
- Has been associated with unexpected serious harm to participants.

Indicate that when research is suspended or terminated by the reviewing IRB that all members of the research staff must comply with the terms of the suspension or termination, including any management plans to ensure that the rights and welfare of research participants are protected. Such actions might be as follows:

- Complying with the IRBs' plan for withdrawing participants at your site and transferring them to another site.
- Informing participants of a termination or suspension of research.
- Reporting any adverse events or outcomes associated with the suspension or termination to the reviewing IRB.

Add to your SOPs:

- The investigator reports all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator's brochure) identifies as not needing immediate reporting. The investigator follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB.
- The investigator reports adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
- For reported deaths, the investigator supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
- The investigator provides written reports to the sponsor, the IRB, and, where applicable, the site on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.
- If the investigator terminates or suspends a clinical trial without prior agreement of the sponsor, the investigator informs the site, sponsor, and the IRB.
- If the IRB terminates or suspends approval of the clinical trial, the investigator promptly notifies the sponsor.
- Upon completion of the clinical trial, the investigator informs the site; the IRB with a summary of the trial's outcome; and the regulatory authority with any reports required.