Tips for Writing the Protocol: How to Avoid Common Errors

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What is a protocol and why is a protocol necessary?

- The protocol provides the IRB with all of the necessary information regarding study design, conduct of the study and execution of the study.

What does a properly written protocol look like?

- A protocol needs to be written so that anyone who reads it has the same takeaway message.
- A properly written protocol will accurately describe the rationale, study design, objectives and plan. It will also include study procedures, management of the data, confidentiality, plans for data analysis, etc.
- The protocol is designed to address specific research question(s)/hypothesis/objective(s).

Which protocol to use?

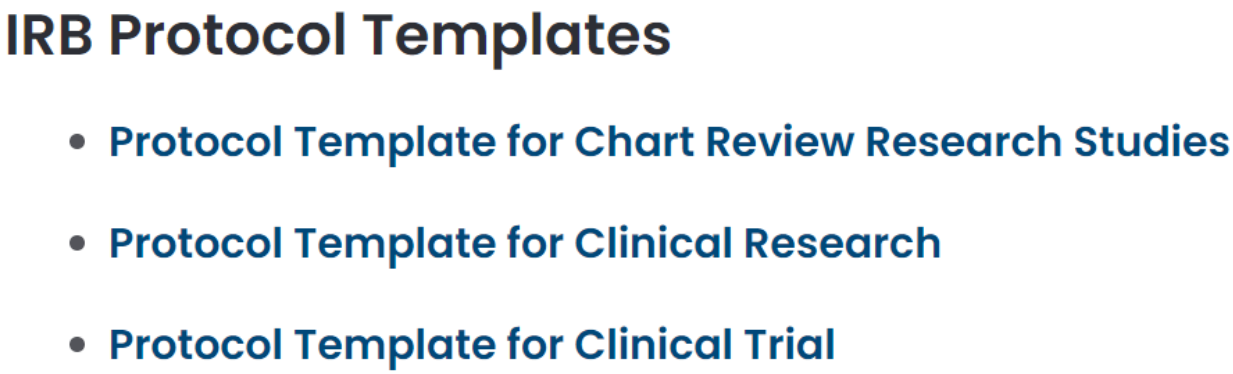
A protocol is required for all CHLA IRB application submissions but sometimes a decision needs to be made about which one to use:

- If a Sponsor's protocol is available, upload the Sponsor's protocol in the iStar application. However, a Sponsor's protocol does not always provide all the information needed (doesn't differentiate research procedures from standard of care procedures, no description of timing and frequency of research procedures, doesn't say if CHLA HIM services will be used, etc.) so it may be necessary for you to create and submit a CHLA supplemental protocol as well.
- If there is no Sponsor protocol, download the CHLA protocol template from the HSPP website and create your own protocol.
- For ceded studies using a central IRB (WCG/Advarra/Sterling IRB), there will be a protocol available from the Sponsor that you will use.
- For ceded studies where an external IRB is the Reviewing IRB (e.g. CHOP IRB, etc.), the Reviewing IRB will provide you with the protocol.

Where to find the CHLA Protocol Template?

- The CHLA protocol template can be downloaded from the CHLA HSPP website.

  https://www.chla.org/research/human-subjects-protection-program-hspp-and-institutional-review-board-irb > Scroll down to the “IRB Protocol Templates” heading



Which CHLA protocol template to use?

- Template for chart review research studies –used solely for a chart review research study.
- Template for clinical research – used for intervention studies that are not clinical trials and do not have a sponsor protocol available.
- Template for clinical trials – Intended for clinical trial studies that do not have a sponsor protocol available.

Best practices for writing a protocol

- Use clear, simple language. The IRB is made up of a diverse group of members from many fields, including community members who do not have a scientific background.
- Use present tense when describing the study so the IRB knows that the research you are submitting for review and approval hasn't already been conducted.
- Past tense can be used when describing relevant prior research, gaps in knowledge, scientific background, significance of the research based on existing literature and how the proposed research will add to existing knowledge.

Common problems

- Missing protocol
- Outdated, retired version of the CHLA protocol is used
- Incorrect protocol template is used (research procedures involve a blood draw, collection of a urine sample, and completion of surveys → an error is use of a chart review template protocol instead of the protocol template for clinical research)
- Required sections of the protocol template are omitted from the final version of the protocol submitted

Protocol writing tips

- Be consistent
- Differentiate between research vs standard of care
- Be complete
- Describe frequency, duration and timing of research procedures
- Provide information about type of data collected
- Provide inclusion/exclusion criteria for all cohorts
- Provide information about blood draws
- Provide information about tissue collection
- Provide information about repository
- Provide information about remote/electronic consent

Protocol Tips: Be Consistent

- Do not rush when it comes to writing the protocol as this can result in an incomplete protocol, a protocol that lacks sound research design and inconsistency.
- Protocol must be consistent with information described in the iStar application, recruitment documents and consent documents.
  - For example: if the protocol describes recruitment using email script and flyers, these recruitment materials must be created and uploaded to the iStar application.

Protocol Tips – Differentiate between research and standard of care

- Be sure to differentiate what procedures are being done for research vs what procedures are being done as part of standard of care (routine care).
- If using a Sponsor's protocol, this information is often not included so you may have to create a CHLA supplemental protocol to explain it.

Protocol Tips – Be Complete

- The protocol must describe procedures for all cohorts and any sub-study that CHLA is participating in.
- Be sure to differentiate standard of care procedures from research procedures for all cohorts and/or sub-study participants.

Protocol Tips - Describe frequency, duration and timing of research procedures

- Describe frequency, duration and timing of research procedures. For example:
  - The subject will be asked to complete surveys either online and/or in person for research purposes at 3 time points throughout the study.
  - The surveys will be completed at week 3, week 6, and week 9, and it is expected that this will take the subject approximately 30 minutes to complete at each time point.

Protocol Tips– Provide information about type of data collected

- If the research is a retrospective chart review study, identify the end date of when the information will exist in the medical records.
- If conducting a retrospective and prospective chart review study, enter a statement in the protocol indicating the study is a retrospective and prospective chart review study. No need to specify a date range.

Protocol Tips – Provide information about type of data collected

- Include a statement to indicate if the study team will use CHLA Health Information Management (HIM).
  - If yes, describe what information will be provided to HIM staff (e.g., ICD and/or CPT codes) and what information will be provided by HIM staff to the study team (e.g. patient names, MRNs).
  - If not utilizing HIMs, indicate this in the protocol.
- The protocol doesn't have to list specific ICD and/or CPT codes.

Protocol Tips – Provide inclusion/exclusion criteria for all cohorts

For studies with:

- multiple cohorts- provide inclusion/exclusion criteria for each cohort
- parent/legal guardian as participants- describe inclusion/exclusion criteria for these participants.
- Age criteria – provide minimum and maximum age of allowable. The IRB reviewer/IRB will need this information to make child-risk determinations.

Protocol Tips – Provide description of the blood draw

If your study involves research blood draw(s), enter the following information in the protocol:

- A description of the method used to obtain the blood draw
  - For example: blood draw is obtained via venipuncture – needle stick for single blood collection, obtained using an existing central venous catheter, obtained using finger stick, obtained using heel stick, etc.
- A description of the timing and amount of the blood to be drawn for research and include scientific and household measurements
  - For example: x mL, x tablespoon or x teaspoon of blood will be collected at one time point only during this study; x mL, x tablespoon or x teaspoon of blood will be collected at several timepoints in this study including day x, week x, and week x; etc.
- A description of how the blood sample is obtained
  - For example: additional blood will be drawn during the subject's standard of care blood draw; additional blood will be drawn only during a standalone blood draw done solely for research purposes; blood sample is being received from an existing repository (provide study number); etc.

Protocol Tips – Provide description of the blood draw (continued)

- Include the reason for performing the blood draw
  - For example: Your blood sample will be taken to perform x testing
- Include whether the blood sample will be used for genetic testing, whole genome/exome sequencing, etc.
- Indicate if results of the blood test done for research will be provided to the participant
- Include statement that all blood draws will comply with the CHLA blood volume policy

Protocol Tips – Provide information about collection of tissue

Describe the collection of research tissue sample(s) in the protocol:

- Specify the type(s) of tissue (i.e. brain tissue) to be collected.
- Describe how the tissue is collected
  - For example: leftover tissue that would normally be thrown away is collected during a standard of care procedure; extra tissue is collected at the time of a standard of care or routine surgery/procedure; tissue is obtained during a nonstandard of care procedure (i.e. biopsy done solely for research purpose); tissue is obtained from an existing repository – specify the CHLA study #; etc
- Add a description of the timing (one-time tissue collection, tissue collected at two time points throughout the study at day x and week x) and add a description of the amount of tissue to be collected.
- Describe what testing is to be done with the tissue. Specify whether this includes genetic testing, including whole genome/exome sequencing.
- Indicate if results of the research tests done on the tissue will be provided to the participant.

Protocol Tips – Provide information about the repository

If the study involves a repository, the following information should be included in the protocol:

- Specify whether a data and/or specimen repository is being created or if an existing repository will be used.
- If a repository is being created, indicate if data/specimens from other CHLA IRB approved studies may be stored in the repository. If submitting data and/or specimens to an existing repository at CHLA, specify the CHLA study # in the protocol.
- Specify the location of the repository
- Describe the reason for having the repository and intended use of the data/specimens stored in the repository
    - For example: The purpose of the repository is to store data/specimens to support the conduct of future research about x condition, support future research about other conditions unrelated to the condition/disease being studied in this particular study, etc. List the data to be stored or associated with each specimen.
- Describe how investigators will receive the data and/or specimens
    - For example: Investigators will receive coded data and specimens to which they will not have the key, anonymous data and specimens (not labeled with study ID#), etc.
- Describe the procedures to release the data/specimens from the repository

Protocol Tips – Provide information about the repository (continued)

- Indicate if future research with the specimens stored in the repository may include genetic testing and/or whole genome/exome sequencing
- Indicate how long data and/or specimens will be stored in the repository
- Refer to the sample language in the “future use of data/specimens” section of the protocol
- Reference the “guidance for future use and repositories” doc

Protocol Tips –Provide information about remote/electronic consent

- Refer to our "**Remote Consent for Research: Obtaining Consent and Documenting Consent (Electronic Consent)**" guidance document on the HSPP website (page 3) and describe the remote consent process and documentation of electronic consent if obtaining remote consent

Sample Statements for Describing a Remote Consent Process (Consent Conference) for Potential Participants

- ☐ The study team will reach out to the participant/parent or legal guardian via phone before the consent discussion to determine if they are interested in participation.
- ☐ If the participant/parent or legal guardian are interested in participating, the study team will make arrangements to email or mail the consent/assent forms, HIPAA authorization form and Experimental Subject's Bill of Rights to them before scheduling a conference call.
- ☐ The participant/parent or legal guardian will receive all documents in advance of the informed consent discussion.
- ☐ The participant/parent or legal guardian will be asked to read over the documents and make note of any questions to prepare for the call.
- ☐ Once the participant/parent or legal guardian has received and reviewed the forms, a conference call will be scheduled for the remote consent discussion.
- ☐ The study team will verify the identity of individuals to ensure the correct individuals are present for the consent conference (i.e., participant/parent or legal guardian).
- ☐ The informed consent discussion will be completed via telephone or video conference (using a CHLA approved, HIPAA compliant platform) just as would occur in-person. A link to the electronic signature platform will be sent prior to the conference call. The participant/parent or legal guardian will be asked to sign and date all forms before ending the call if they choose to participate. Instructions for returning the signed documents will be discussed.
- ☐ If additional time is needed for the participant/parent or legal guardian before signing the forms, an additional phone call or video conference will be scheduled.

Protocol Tips –Provide information about remote/electronic consent (Cont'd)

Sample Statements for Describing Documentation of Consent (Electronic Consent):

- ☐ When the consent information is presented in an electronic format, the e-consenting system will be designed so it is easy to navigate and allow the participant/parent or legal guardian to proceed forward and backward within the document, as well as allow the participant/parent or legal guardian to pause for later review and continue later.
- ☐ After obtaining informed consent, the participant/parent or legal guardian will be instructed how to sign the consent documents electronically. Only CHLA approved, HIPAA compliant platforms will be used to document electronic signatures. The correct areas for signatures and dates will be flagged to ensure all required signatures are obtained.
- ☐ The study team will ensure the consent/assent forms are signed by the correct individuals who participated in the consent conference (i.e., participant/parent or legal guardian).
- ☐ The consenting study team member will countersign the consent/assent and HIPAA forms and document the consent conference in the study files, being sure to document the name of any witnesses and the means of communication.
- ☐ Copies of the fully signed forms will be emailed or mailed to the participant/parent or legal guardian.
- ☐ All of the above steps will be completed prior to the start of any study procedures (e.g., screening procedures) with the participant.
- ☐ *Be sure to also describe how subjects will have access to all of the consent related materials, including hyperlinks or other external documents throughout the lifespan of the study.*