Submitting Amendments

Tea with the IRB

Maryann Girgis, BA, CIP

September 19, 2023

11am – 12pm

CHLA HSPP IRB Website

https://https://www.chla.org/research/hspp

Bookmark it and visit regularly!

Related Guidance Document

Amendments to CHLA IRB Approved Research

Use this presentation as a “How to”

Goals

- A better understanding of how the IRB reviews amendment submissions.
- Learn what the IRB expects to see in an amendment application.
- Learn how to submit a complete amendment application.

General Rule

- All modifications to the study must be submitted, reviewed and approved by the IRB before implementation (except in the case of preventing immediate harm/hazard to a subject).

Examples of Minor and Major Amendments

- These examples are provided as guidance for investigators, but the IRB will make the final determination of whether an amendment is minor c major.

MINOR AMENDMENTS	MAJOR AMENDMENTS
☐ Administrative changes ☐ Minor consent form changes ☐ Minor changes to recruitment procedures, recruitment materials or submission of new recruitment materials to be used in accordance with approved recruitment methods ☐ Minor changes to study documents such as surveys, questionnaires or brochures ☐ New study documents to be distributed to or seen by subjects that are similar in substance to those previously approved ☐ Changes in payment to subjects or the amount subjects are paid or compensated that are not significant enough to affect the risk/benefit ratio of the study ☐ Decrease in the number and volume of sample collections as long as they do not negatively alter the risk/benefit ratio of the study ☐ Editorial changes that clarify but do not alter the existing meaning of a document ☐ Addition of or changes in study personnel ☐ Addition of a new study site (in many but not all cases) ☐ Translations of consent and assent documents already reviewed and approved by an IRB	☐ Changes that affect the risk/benefit ratio of the study or specifically increase the risk to subjects ☐ Changes in inclusion/exclusion criteria that impact the risk/benefit ratio of the study ☐ Significant changes in study design, such as the addition of a new subject population or the elimination of a study arm ☐ New risk information that is substantial or affects the risk/benefit ratio of the study ☐ Addition of a new study drug or device ☐ Significant changes to the study documents to be distributed to or seen by subjects ☐ New study documents to be distributed to or seen by subjects that include information or questions that are substantively different from materials already approved by the IRB. ☐ Changes to the PI of the study ☐ New or revised financial conflict of interest management plans for study team members (PI, Co-PI, key personnel)

Most Often Submitted Amendments

- Funding
- Informed Consent and/or Addenda
- Investigator's Brochure / Package Insert
- Number of Subjects
- Procedures and/or Protocol
- Recruitment Materials
- Subject Population
- Subject Reimbursement / Compensation
- Study Personnel

Winning Formula

Description of changes/revisions/updates

+

Rationale for the changes/revisions/updates

=

SUCCESSFUL AMENDMENT SUBMISSION

iStar Amendment Application

- Funding – Item AM4
  - Example Description
    - Adding/removing funding sources
    - Changes to Sponsor
  - Example Rationale
    - Because PharmA acquired the study drug from PharmB, PharmA is now sponsoring the study
  - Revisions to iStar application items 4.1, 4.4, consent/permission documents (items 24.7 & 24P.5) , possibly items 24.2 (recruitment materials), and 25.1(financial obligation)
    - If the study is no longer receiving federal funding, do not remove funding information from item 4.1. Instead, revise item 4.4 or item 40.2 to indicate "formerly funded by (insert federal agency)."

iStar Amendment Application

- Informed Consent and/or Addenda – Section AM5
  - Item AM5.1: Summarize changes and provide rationale
    - Simplest description method: bullet points
    - Example rationale: For consistency with the newly revised protocol and Investigator's Brochure, the consent forms have been revised to reflect the new procedures and risks.
    - This could also include assent and permission form changes
  - Item AM5.2 : Indicate whether there have ever been subjects enrolled into the study.
    - Yes or No, there is no maybe

iStar Amendment Application

- Informed Consent and/or Addenda – Section AM5 (cont.)
  - Item AM5.3: Should enrolled or previously enrolled subjects be informed of the changes?
    - Informing does not always mean re-consent
    - Are any subjects currently enrolled?
      - If any subjects are currently enrolled, are they in the cohort that is affected by the revision?
    - What phase are the study subjects in? (i.e. treatment, long-term follow-up, etc.)
      - Example: All CHLA participants are in long-term follow up, but the newly identified risk of anemia only affects those receiving treatment.
    - New risk? Is the new risk something that will only affect subjects currently undergoing study procedures or could it impact subjects long after they stopped study procedures?
    - Do minor revisions require informing subjects? (i.e. change in PI, new data collection variables from medical record, etc.)

iStar Amendment Application

- Informed Consent and/or Addenda – Section AM5 (cont.)
  - AM5.3.1: How do you plan to inform subjects?
    - Verbal Disclosure
    - Addendum Consent/ New (additional) Informed Consent
    - Revised Informed Consent/Information Sheet
    - Letter Notification (especially for late effects)
  - When deciding on how to inform subjects, some things that should be considered are:
    - Significance and extent of the revisions
    - What phase of the study the subjects are in and the status of the study
    - Is this new information anything they could execute (i.e. stop taking the study drug or get more frequent monitoring for late effects)

iStar Amendment Application

- Informed Consent and/or Addenda – Section AM5 (cont.)
  - Item AM5.3.2: Explain who will do this and when it will be done
    - Who? (i.e. PI, Co-I, study coordinator, etc.)
    - When? (i.e. next clinic visit)
    - How? (i.e. in-person, over the phone, etc.)
  - Item AM5.3.3: Explain why participants need not be informed
    - Example: Updated HSPP template language – The revisions made to the consent form do not provide new information and do not affect the participants decision or willingness to participate.
      - However, some template language changes are substantive, so consider the impact of the template language change before assuming subjects need not be informed.
        - Example: Change in laws regarding sexual and reproductive health care disclosures
  - Revisions to iStar application items 24.7, 24A.4, and 24P.5 (consent/assent/permission documents)

iStar Amendment Application

- Investigator's Brochure/Package Insert – Section AM6
  - According to HSPP policy, changes to the Investigator's Brochure must be submitted by the Principal Investigator.
  - Revision to iStar application item 17.2, and possibly item 17.1, the consent/assent/permission documents (items 24.7, 24A.4, and 24P.5), and items 27.1 & 27.2 (risks)
    - If the IB does not have an embedded section with a summary of changes, the PI must submit a separate summary of changes document, obtained from the sponsor.
    - If the IB version submitted is not the next one in sequence (i.e. the IRB reviewed v5.0 and now you are submitting v7.0), please provide an explanation for why v6.0 was not submitted (i.e. "IB v6.0 was created to meet the regulatory requirements of the European drug agency. The Sponsor directed the study team that it was unnecessary to submit to US IRBs") and upload any supporting documents (such as memos from the sponsor) that provide an explanation to item 40.1

iStar Amendment Application

- Number of Subjects – AM7
  - Describe each change to the number of subjects
    - Example: Increase number of subjects from 10 to 20
  - Rationale for the change
    - Example: Increase power of the study
    - Example: More subjects eligible for enrollment than anticipated (for repository studies)
  - Revision to iStar application item 10.1 and possibly items 10.1.1 and 1.4.

iStar Amendment Application

- Procedures and/or Protocol – AM8
  - Describe the nature of the changes to the protocol, procedures, or methods
    - Bullet points describing the main/most significant revisions
    - If applicable, refer to an uploaded summary of changes document (not track changes)
  - Describe the rationale for the changes to the protocol, procedures or methods
    - Example: We have determined that a medical chart abstraction will not provide us with a thorough understanding of obstacles to patient care; therefore, we are now including a patient survey
  - Revisions to iStar application items 1.4, 5.2, 24.2 (recruitment materials); 24.7, 24A.4 & 24P.5 (consent/assent/permission documents), and 27.1 & 27.2 (risks)
  - If the protocol does not have an embedded section with a summary of changes, the PI must submit a separate summary of changes document, obtained from the sponsor.

iStar Amendment Application

- Recruitment Materials – AM10
  - Typically, recruitment materials are revised to reflect the changes made to study procedures, contact information, and/or compensation
    - For newly added recruitment materials, provide a description of the new recruitment tool and how it will be used.
      - Example Description: We have developed a recruitment flyer that will be handed out by study team members at the CHLA Farmer's Market
      - Example Rationale: In order to reach more subjects from the community, we have decided to post flyers at local YMCAs.
  - Revisions to iStar application item 24.2 and possible items 24.1 and 24.1.2.
  - Keep in mind that revised recruitment materials should still reflect the basic dos and don'ts listed on the HSPP website (https://www.chla.org/research/hspp → Recruitment, Consent and Assent → Identification and Recruitment of Research Participants)

iStar Amendment Application

- Subject Population – AM13
  - Example Descriptions
    - Include younger and/or older participants
    - Include control arm and/or new cohort
    - Include Parents/Legal Guardians
    - Include Adults Not Competent to Consent
  - Example Rationale
    - In order to thoroughly understand the impact of patient diagnosis, we would like to also survey parents/legal guardians about what aspects of their life have been affected
  - Revisions to iStar application items 1.4, 5.2, 10.2, 10.3, 10.3.1, 24.2 (recruitment materials); 24.7, 24A.4 & 24P.5 (consent/assent/permission documents), and 27.1 & 27.2 (risks)
  - The addition of a new cohort with different inclusion/exclusion criteria than the current subjects also constitutes a change in subject population.

iStar Amendment Application

- Subject Reimbursement/Compensation – AM13
  - Include in the description
    - How much? ($USD)
    - In what form? (i.e. cash, gift card, check, ClinCard, etc.)
    - When? (i.e. at the end of each visit)
    - Issued to who? (i.e. all subjects regardless of age, parents/legal guardian of minor participants, etc.)
  - Example Rationales
    - Because we have lost funding, subjects will now receive $10 cash instead of $20 cash.
    - Because psychological testing will take 3 hours to complete and time off work, subjects will receive $100 cash.
  - Revisions to iStar application items 25.2, 24.2 (recruitment materials), and 24.7, 24A.4, and 24P.5 (consent/assent/permission documents)

iStar Amendment Application

- Study Personnel
  - Add/remove study personnel
  - Change study personnel roles
  - Change consenting privileges
  - The only amendment type that does not have a corresponding AM summary section
    - However, there is a prompt in the amendment application to edit item 2.1 in the iStar application
  - Revision to iStar application item 2.1
    - If the PI of the study is being changed, this will also require revisions to item 24.2 (recruitment materials) and the consent/assent/permission documents (items 24.7, 24A.4, and 24P.5)
      - If Co-Is are changed or removed, the “Introduction” section of the consent/assent/permission documents may also require revision

In Conclusion

- Select the type of amendment
- Describe the amendment changes
- Provide the rationale for the changes
- Change the iStar application items and uploaded study documents
  - Use “Add” function for new documents
  - Use “Upload Revision” function for revisions/updates to existing documents
    - This function can be accessed by selecting the ellipses (•••) next to the document

Q&A

???

The End

Thanks for your time

Don’t forget to visit the CHLA HSPP IRB website!

☺ ☺ ☺