How to Draft a Modification Summary of Changes

All modification submissions require a summary of changes document that outlines all changes and provides rationale for each revision. Please review the guidance below for developing an appropriate summary.

Provide Revision Listings Per Document:

- Provide an overall list of all documents being revised with the modification
- If there are new documents being added along with revisions to approved documents, please differentiate in the cover letter or summary document to avoid confusion
  **For new documents, provide an explanation for why they are being added to the study with the modification*

Explain the Revisions AND the "Why" Behind the Revisions:

- **For each document being revised**, provide A) the list of revisions, AND B) associated rationale/justification for substantial revisions
- **DO NOT RELY on Sponsor summaries:** The summary of revisions from the Sponsor is often a good tracking mechanism or table of contents for the revisions but is often lacking specific rationale and explanation of the impact of the revisions (this will be requested from the PI/Study Team to process the modification if not provided). Likewise, it is the study team's responsibility to review the summary of changes, identify the substantive changes, and highlight those for the IRB in the cover letter or modification form.
- Things to think about when writing the summary of revisions:
  - Why is the change being made at this time?
  - What are the implications of the change?
  - Will current participants be affected by the change?, and
  - Do the revisions propose any changes that might overall affect the risk/benefit ratio and criteria for IRB approval as currently assessed for the study?

Separate out logistical/administrative revisions from substantial ones:

- **Logistical/administrative/editorial** revisions can be simply noted to be tracked in the updated protocol/consent form/HS-ERA application/etc. The rationale for this is that these types of revisions do not require rationale or detailed explanation, while substantive revisions do.
- **Clarifications / corrections** should be identified because at times they may be identified as a substantive change under some circumstance. However, rationale is not necessary.

Consider Needs for Re-Consent:

- If there are any subjects on study when the modification is submitted, and there are revisions to the consent form or other substantial revisions, a plan for whether the revised/updated information will be shared with the current subjects must be provided and justified.
- When the risk section of the consent form is impacted, consider whether subjects in follow up need to be apprised of new non-acute risks.

Identify the Level of Review

- If the revisions are being proposed to qualify for expedited review (not requiring review by the convened board), provide sufficient rationale as to why the revisions (especially if substantial/comprehensive revisions) do not warrant convened review (e.g., the revisions don't impact the Penn participants, revisions align with previous determinations made by the convened board, revisions do not require physician level review, revisions do not impact IRB criteria for approval, etc.)

Revisions that the IRB will identify as needing convened review include the following:

Type of Change	Why Convened Review is Required The IRB will need to assess whether the…
• Revisions to the IB section Summary of Data and Guidance for the Investigators that impact the risk language in the consent form and /or may impact a subject's willingness to participate	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Proposed monitoring plan continues to appropriately protect subject safety.
• Substantial protocol amendments:	
○ Increase in target enrollment for early phase (first in human, Phase 1-2) research	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Whether the proposed monitoring plan continues to appropriately protect subject safety.
○ Significant increase in target enrollment for an investigator-initiated greater than minimal risk protocol	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Proposed monitoring plan continues to appropriately protect subject safety.
○ Significant changes to the protocol design (impactful on criteria for approval)	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Proposed monitoring plan continues to appropriately protect subject safety.
○ Significant changes to the selection criteria	• Risks to subjects are still minimized • Subject selection is still equitable • Risk benefit ratio is still appropriately balanced • Proposed monitoring plan continues to appropriately protect subject safety for any newly identified populations. • Additional protections are needed for vulnerable populations
○ Introduction of new procedures that do not qualify for expedited review under the designated expedited review categories (e.g., biopsy, CT scan, X ray, MRI with contrast, etc.)	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Whether the proposed monitoring plan continues to appropriately protect subject safety.
○ Substantial change to study product (design, formulation, dosing, preparation, administration, etc.)	• Risks to subjects are still minimized • Risk benefit ratio is still appropriately balanced • Whether the proposed monitoring plan continues to appropriately protect subject safety.
• Adding a non-significant risk medical device used in an investigational manner to a protocol	Medical Device Risk Determinations can only be made by a convened board.

Other Helpful Tips

- Summary of Changes made be provided in the IRB Modification Form, or they can be provided within a cover letter or another standalone document.
- Consider source of revisions from the IRB perspective; if you are adding information to the protocol and/or consent form and don't have documentation to support where the new information is coming from, please explain the source/rationale for the revisions in order to assist the IRB in the review/approval process
- Before submitting the modification to the IRB, review your list of revisions against your tracked copies/other updates to be sure that the submission is complete

Administrative Requirements for Amendments:

- Please provide both tracked and clean copies of all documents to facilitate IRB review, including protocols, informed consents, IBs, and other participant facing materials.
  **Note: If a Sponsor declines to provide a tracked document, please note this in the summary. Further summary/explanation of revisions may be required by the IRB in order to process the modification.*

- If the study is greater than minimal risk, a document list will be required for the IRB correspondence letter or modification form. This listing should be in a format that the IRB may copy and paste into the IRB approval letter. An example of an appropriate document listing:

  -Modification Request Form, dated 1/1/2020
  -Cover Letter, dated 1/1/2020
  -Protocol version 8, dated 1/1/2020, tracked and clean
  -Protocol version 8, SOC, dated 1/1/2020
  -Product Name IB, version 10, dated 1/1/2020
  -Main ICF, version dated 1/1/2020, tracked and clean
  -Screening ICF, version dated 1/1/2020, and clean