Amendment submission DO's and DON'Ts:

This guidance document is intended to help researchers avoid the common pitfalls that result in delays to the review and approval of amendment submissions. Careful adherence to each of the following points will help researchers to prepare amendment submissions that can be easily understood and therefore processed by the HREB. *Amendments that are not adequately documented or readily understandable cannot be reviewed, leading to delays in approval decisions.*

1) ***DO:*** *Provide a clear, detailed but concise description of the amendment in Section 2.0 of the PAA form.*

The response in Section 2.0 of the PAA either includes too much detail (ie. copy and paste verbatim from listing of changes in attached protocol) or no detail at all. Section 2.0 of the PAA form should provide a clear, detailed but concise response to:

a. describe the nature of the proposed change(s); describe any changes to the study, involving the study's objectives, research design, sample size, inclusion/exclusion criteria, and/or changes to the treatment/intervention procedures/dosage and explain how any changes will affect the study;
b. clearly describe the ***rationale*** for these changes; and
c. whether these changes impact the risk/benefit profile of the study or how these changes impact participants.
d. If the changes will result in any increase in risk or discomfort for the study participants, explain what these are and why the changes are required.

NOTE: The thing most often missing when amendments are submitted is a clear description of WHY changes have been made (rationale) and how this may (or may not) impact participants. A summary statement at the end of Question 2.0 – that provides the Investigator's opinion as to how the sum of the proposed changes to the protocol impact the overall risk/benefit ratio of the study – greatly facilitates this understanding by REB reviewers.

2) ***DON'T:*** *simply copy and paste from the Protocol Summary of Changes.*

While you are very familiar with the details of your protocol, copying and pasting a large bulleted list of changes with no context does not help the HREB understand the substance of your amendment. The HREB reviews over 800 amendment submissions each year. Given this volume a full review of the Protocol and all attached documentation is not an efficient use of REB resources. The PAA form (like a cover page) is intended to summarize the substance of the amendment and outline important changes that will impact the welfare of participants in the study and highlight where these changes are outlined in attached study documentation as required.

3) ***DO:*** *Update all sections of the study application that are affected by the proposed changes.*

Any changes contained in the amendment that affect existing sections of the approved application MUST be updated. Examples of updates often required are:

- Changes to recruitment methods in 4.3 or 4.4
- Changes to inclusion/exclusion criteria in 4.2
- Changes to risk information in 3.1 (3.0)

- Changes to methods or procedures in the study in 2.1 (4.0)
- Addition of a new sub-study in 2.1 (7.0).
- Changes to consent document – revised document (clean and tracked change version) uploaded to Documentation section.

Ensure the changes you have made are consistent across all documents, so revisions within the protocol are reflected in consent form(s) *and* in the study application. Conversely, all changes made to consent forms and the study application should be justified, and reflected in the protocol.

4) ***DO:*** *Check to see if Health Canada approval is required for your amendment.* (Question 5.0: Is Health Canada approval required for this amendment?)

If the study is regulated by Health Canada, any changes to a protocol need to be reviewed/approved by Health Canada. Depending on the nature of the protocol changes, as outlined below, Health Canada may or may not issue an approval letter. As applicable, Health Canada's approval letter must be submitted to REB before the updated protocol can be approved.

a) Per Health Canada, the following changes must be approved by Health Canada before they can be implemented:
   - affect the selection, the criteria for selection, monitoring, or dismissal of a clinical trial subject
   - affect the evaluation of the clinical efficacy of the drug
   - alter the risk to health of a clinical trial subject
   - affect the safety evaluation of the drug extend the duration of the clinical trial

   Health Canada will issue an approval letter, which must be submitted to REB before implementation. (In this case, #5.0: Is Health Canada approval required for this amendment is "Yes".)

b) Per Health Canada, the following changes can be implemented immediately, but Health Canada must be informed in writing via a notification:
   - changes to the protocol that do not affect the safety of the trial participants and which would not be considered an amendment
   - information on site closure or completion of the Clinical Trial
   - when the Clinical Trial has been discontinued in its entirety or at any clinical trial site for reasons not related to the safety of clinical trial participants (e.g., for administrative purposes, lack of recruitment, etc.)
   - changes to Quality (Chemistry and Manufacturing) information that do not affect the quality or safety of the drug

   Health Canada will review the Notification but will not issue an approval letter or acknowledgement (#5.0: Is Health Canada approval required for this amendment = No). In this case, the REB will request written confirmation from the Sponsor that a Notification was sent to Health Canada.

5) ***DO:*** *Clarify if you have participants enrolled in the study*

The questions related to participant enrollment in the amendment form allow the HREB to determine how new information is going to be presented to participants. These questions

are often not answered, or answered incorrectly. Where there are participants already enrolled in the study, a consent addendum – which ***only*** provides new information, is needed. If no participants are currently enrolled in the study, then it would be ok to only provide a fully updated consent form for review. The consent addendum template outlines the HREBs suggestions on how to provide new information to participants currently enrolled in the study. Please ensure that your amendment and uploaded documents comply with this document (see "Addendum to Consent").

6) ***DON'T:*** *forget to rename your new uploaded documents.*

If you are uploading new documents in the Documentation Section (using the "Upload Revision" button) – remember that the online system will ***not*** rename the new document automatically. The system is set to keep the old document name. The consent form name is linked to the approval letter – so if the version date of the document does not match the version date in the name of the document, we will have to send the amendment back to you to update it (see "Change Document Title").

7) ***DO:*** *provide a clean and tracked change copy of all revised documentation (as applicable).*

Knowing what specifically has changed is very important for the review of an amendment. If the reviewers cannot easily see changes, reviewing an amendment becomes very difficult and takes much more time.

8) ***DO:*** *provide a complete and accurate listing of the documents AND VERSION DATES that have been submitted for review and need to be acknowledged in approval letters.*

Listing ALL documents and their correct version dates will allow the HREB Specialist to copy and paste this listing into an approval letter. This greatly saves us time and reduces the risk of any transcription errors for the approval letter.

9) ***Finally…..DON'T:*** *expect the REB Specialist to write your amendments for you. Submissions which do not adhere to the points above will be returned to you and result in delays to the approval process.*

If you have any difficulties using the online system, please contact the Research Ethics Office at reoffice@ualberta.ca or 780-492-0459. Visit our website: uab.ca/reo.