Mass General Brigham

Modifying an Existing Study vs Submitting a New Study

All changes in approved research must be reviewed and approved by the IRB prior to implementation. When proposing changes to an existing study, investigators and the IRB should consider whether the changes warrant submission of a new study rather than an amendment. It is necessary to assess submissions on a case-by-case basis. It is ultimately up to the IRB to determine when a new study will be required. This guidance applies to all research studies overseen by the Mass General Brigham IRB including those under Single IRB Review.

We also encourage you to discuss your proposed changes with the IRB prior to submitting an amendment. IRB contact information can be found here.

Some examples of when a new study must be submitted:

- For Single IRB studies, addition of new aims, hypotheses, populations, or shift in study design or research question for any site must be submitted as a new study. Of note, if there are new aims, hypotheses, or a change at a non-MGB site, this could potentially require a new submission at that site's respective IRB.
- Developing a medical device typically includes multiple stages. The first stage is to develop a prototype and test usability. The next stage is to test the safety and effectiveness of the prototype with a small group of patients. The final stage is to conduct a randomized trial. In this scenario, even though the overarching aim is consistent (i.e., to develop a medical device), it is best to submit three separate studies, rather than submitting amendments to the original study. This permits appropriate regulatory determinations to be made for each portion of the research.
- Adding new investigational drugs, medical devices or procedures that are FDA regulated to a study which has not previously been FDA regulated requires a new study. The devices or drugs may impact the overall study design and research focus as well as study procedures and the overall consent form. The IRB will need to make determinations about the use of the investigational device or investigational drug in the study, which may now be subject to FDA regulations.
- Multiple sub-studies embedded within one study can be difficult to review and track for compliance over time. If the hypotheses, aims, populations, procedures, and/or funding source of sub-studies differ from the main study, the sub-study should be submitted as a new study.
- Requests to utilize data or samples from repository and registry studies to conduct human research projects (e.g., new analyses on identifiable samples or data) requires a new study submission to the IRB. Investigators sometimes modify existing repository and registry studies to include new investigators who may have their own funding and seek to use the data or samples from these studies to conduct a secondary analysis study, but this is not permitted since it increases the recordkeeping and compliance burden of the repository/registry owners and alters the original repository/registry protocol intent and structure. Rather, standalone secondary use studies which are limited in scope to the use of samples and/or data obtained

during a previous research study should be established. These new studies using existing data or specimens must be submitted for IRB review and approval.

- Significant modifications to older studies may require reconsideration of risks and benefits of the study (e.g., new standards of care may have been established since the time the study was initially approved) and may need to be submitted as a new study. In addition, studies that have been open for an extended period may include irrelevant or outdated information as portions of the research may be complete and this can create confusion about what activities are ongoing.
- If the proposed changes result in a "menu" of procedures that may be used, for instance, if there is a separate set of inclusion/exclusion criteria for different procedures and different risk profiles need to be considered in the consent form, the IRB finds it difficult to assess the risks of the research to individual participants. The IRB will need to consider all possible combinations of procedures for all possible participants, and an amendment could lead to multiple rounds of revisions and a longer time to review than a new study. In addition, studies with "menus" are difficult for study staff to execute compliantly, present challenges to proper recordkeeping, and lead to complexities in data analysis and results reporting. In this case, a new application would be advisable.
- Note: New studies must be registered separately on clinicaltrials.gov if they meet the requirements for registration rather than being added to existing clinicaltrials.gov record.

Some examples of when changes can be submitted via an amendment:

- Changes to recruitment materials or methods (e.g., using flyers to advertise to participants), or other documents used with participants (e.g., interview guides, substituting one questionnaire with another).
- Adding payment or modifying the amount participants are paid.
- Changes in inclusion or exclusion criteria without changing the overall study aims or design.
- A study is federally funded, and an investigator obtains an NIH-supplement to add a specific element to that study. The original funding is still necessary to complete the study and although the supplement adds a new hypothesis, procedure, and funding, the study population and overall design remains the same.
- Modifications to current study procedures (e.g., increase in radiation exposure, adding audio recording) when the modifications do not result in significant changes to the study design.
- Adding or removing study personnel.
- If changes do not significantly impact aims, hypothesis, procedures, or study populations, then an amendment may be submitted.

Consider the questions below when deciding whether to submit an amendment or a new study.

Question	Submit New Application	Submit Amendment

Do the proposed changes alter the research aims/purpose, hypotheses, study design, or population? Considerations: • The IRB must assess the risks and benefits of the research. If the research question, design, or population has significantly changed then this is likely to impact the risks and benefits of the study. • Consider the impact of proposed changes on the ability to accurately report study progress/results. If the proposed changes will make progress reporting at Continuing Review, on ClinicalTrials.gov, or to the FDA unworkable, then a new application for a separate study may be required.	• Changes that significantly alter the study aims/purpose, data analysis plans, procedures, or overall study design • Changes that modify <u>more than one</u> of the following: study aims/purpose, study procedures, and study population. Keep in mind that submitting multiple amendments over time that change more than one of these aspects should be submitted as a new study. • New research questions that emerge from knowledge gained in an existing study should be submitted as a new study.	• Minor changes that do not significantly alter the overall study objectives/aims/purpose, data analysis plans, procedures, or overall study design
What changes will be made to the study procedures or methods? Considerations: • If the changes to the procedures or methods are significantly different from the ones already approved in the existing study, assess why it is necessary to make the proposed changes to the procedures/methods. Significant changes in the procedures/methods may mean you are trying to address changes/shifts in the study aims and may require a new study • In addition, the original study can morph into a new study over time (e.g., changes/shift in the original aims, procedures, populations) consequently impacting the clarity and quality of research data. This can also cause confusion and errors among research team members,	• If the proposed procedures or methods deviate significantly from those approved in the existing research study, then a new application should be submitted.	• If the procedures or methods remain the same, or do not significantly alter the study design, then an amendment is permitted.

leading to non-compliance and/or impacting risks to participants.		
How long has the study been open? Considerations: • If the research has been active for several years, the information contained within the study can become outdated as clinical procedures, research regulations, and IRB and institutional policies change.	• Significant modifications to old studies may require reconsideration of risks and benefits of the study. • In addition, studies that have been open for an extended period may include irrelevant information as portions of the research may be complete and this can create confusion about what activities are ongoing. • As new risk information becomes available, studies that have been ongoing may not reflect the most current information. A new application would allow the protocol to be refined to meet the aims of the current research objectives, to include current standard of care, risks, regulatory considerations, and institutional approaches and policies, and to ensure it will reach completion.	• If the study is operating within the planned research timeline and if changes are otherwise not significant, then submitting an amendment is appropriate.
Will the study utilize new funding and/or require a new contract?	• If new funding changes the aims and research design of the project, adds new population, or procedures that significantly differ from the current study, a new application must be submitted. • In addition, whether the funding changes or not, the execution of a new contract with updated terms could result in the need for submission of a new application.	• If new funding is awarded to support the research as currently approved, then an amendment is appropriate.