Dartmouth Clinical Trials Office (CTO) Process for Review of Protocol Amendments

1. A protocol amendment is reviewed by the research staff to determine if the amendment requires scientific review or CTO review.
    - CTO review is required when the amendment results in a revision to the MCA billing plan.
        - The following are examples of protocol revisions that require CTO review:
            - Addition/change/deletion of billable services
            - Addition/change/deletion of visits
            - Addition of inclusion/exclusion criteria that requires services to be added to a screening visit, e.g., HIV screening, HEP B, HEP C, chemistries, hematology
            - Addition/change/deletion of footnotes
        - The following are examples of protocol revisions that do not require CTO review:
            - Dosage/formulations/storage of study drugs
            - Administrative revisions, e.g., revision to personnel, addresses
            - Inclusion/exclusion criteria, e.g., prior medications, histories, revisions to lab test results
            - Drug storage conditions
            - Survival follow-up requirements that are non-billable
            - Study questionnaires
2. The research staff submits the protocol amendment electronically to the CTO via the Amendment Submission Form (ASF). The CTO requests that research teams submit the amendment documents as soon as they are available and in advance of CPHS submission when possible.
    - The following documents need to be submitted to the CTO:
        - Amended protocol
        - Summary of protocol revisions (if available)
        - Sponsor-approved, revised model consent form
            - All appropriate fields in the ASF need to be completed. Special attention needs to be given to the following:
                - The anticipated date of CPHS submission informs the CTO's workflow, so this date needs to be as accurate as possible.
                - The "Special Situation Reviews" box is to be checked if the study's enrollment is suspended until the amendment is CPHS approved or if there are substantive informed consent revisions that will require reconsent of participants or those enrolled during amendment review.
                - If the study's enrollment is suspended until the amendment is CPHS-approved, the research staff will

work to have other CPHS amendment documentation completed and signed while the CTO's review is taking place.
        - The ASF "Questions or Comments" box should include a description of the anticipated revisions to the MCA; this is particularly helpful if there are numerous revisions to the protocol. Other informative notes may be included here as well.
    - If applicable, when a revised sponsor-approved local consent form is available at the time of the ASF submission, it is attached to the ASF. If the protocol amendment requires a revision to the informed consent document concurrent with the CTO review processes, the research staff revises the CPHS-approved consent and seeks sponsor approval as required.
3. Concurrent with the submission to the CTO, the research staff will send the amended protocol, revised informed consent document and other required documents to the CPHS as part of the amendment submission.
4. The CTO reviews the submitted documentation. Within 3 business days the CTO will respond to the research team to inform the team if revisions to the MCA are required.
    a. If the CTO determines no revisions to the MCA are required, no additional review by the CTO is required and the research team can proceed with other amendment activities.
    b. If the CTO determines a revision to the MCA is required, the CTO will begin the work of processing the protocol amendment.
5. The CTO routes the amended MCA to the research team for review and PI approval/signature. The research staff returns the signed cover page to the CTO via interoffice mail.
6. The CPHS notifies the CTO when the amendment is approved. The CTO receives the CPHS-approved informed consent document and the CPHS approval letter.
7. The CTO will perform the final consistency check of the amended MCA, contract, budget, and informed consent document. If during the final consistency check, substantive revisions are identified, a revised MCA may need to be re-routed for review and approval; if the informed consent document is effected, it will need to be submitted to the CPHS for review and approval.
8. Upon receipt of the signed cover page, the CTO will upload into Velos the CPHS-approved, signed MCA.