2024 Application Instructions

Before applying you must agree to the following:

This course requires:

- **An ongoing time commitment from you**
- **Ongoing support from your mentor/supervisor. This may include a 15-minute meeting with your mentor prior to admittance to the course**
- **In-person attendance at the residential course in Charlottesville, VA, from June 3-6**

February: Applicants who are being considered for the course may be contacted to schedule a brief meeting between a course director and your mentor. The purpose of this meeting is to ensure your mentor has full understanding of the course.

Spring/Summer: You will be assigned to a small group that will start meeting in late March; the frequency of meetings is approximately every two weeks with expected deliverables for each meeting. In addition, **attendance at the Residential Course (June 3-6 in Charlottesville, VA) is an expectation if you are accepted into the course** *(travel within the US is compensated)*. Additional preparation and time are expected during the Residential Course so that you can make the most progress while you are there.

Application Instructions:

We are committed to training individuals from underrepresented racial and ethnic groups as well as individuals with disabilities. Please review the website and consult the FAQs and email ninds-ctmc-info@umich.edu with any questions.

Applications are due by 9AM Eastern Time, March 4th, 2024

You should submit your application with all required documents in a single PDF at the following portal: https://redcapproduction.umms.med.umich.edu/surveys/?s=PAFHDEDMJX

Applicants from a clinical discipline who are designing a clinical trial are ideal applicants. This course defines a clinical trial as a research project that delivers an intervention (drug, device, diagnostic, behavioral) to patients in a prospective way.

While most applications are expected from individual investigators, coordinated applications from multidisciplinary teams of investigators with complementary expertise working on a single project will also be considered (2-3 people maximum -clinician and statistician and/or engineer). If selected, ALL team investigators are required to participate fully in ALL course activities. Each team member should submit a separate application, but parts 1 and 2 (see below) should be exactly the same.

2024 Application Instructions

REQUIRED Items for Application Form:

Do NOT use less than 11-point font. Do not adjust the margins. All text (including references) should be included within the specified page limitations. You should delete this text and all instructions; a template is provided at the end of this form.

ATTN Applicants Submitting Revised Applications: For those who have applied previously and are re-submitting a revised application you may include one additional page to your application titled *Revised Application*. This page will be placed before Part 1A (described below). The Revised Application page will describe the feedback you received from the prior application process and other changes you have made to the current application.

Part 1A: Statement of Scientific Area and Key Information *(Limit 1 page including references)*

The goal of the course is to help you develop a rigorous and thoughtful scientific protocol. In the text box provided, discuss the area of study where you will develop a clinical research trial proposal. The most highly weighted criterion is a research project that delivers an intervention (drug, device, diagnostic, behavioral) to patients in a prospective way. Describe potential scientific questions and briefly inventory areas of important scientific uncertainty in the field. This intervention should have a good basis in biology (or theory, for behavioral interventions). Provide a general description of what sort of trial design you think might be appropriate. Provide a critical summary of the existing preclinical or prior clinical work that supports the evaluation of this therapy. Specifically address the rigor and reproducibility of the methods of preclinical experiments that justify implementing your proposal in a clinical trial.

Consider the NINDS Transparency in Reporting Guidelines when drafting this section and discuss the scientific premise underlying your idea:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3511845/
http://www.ninds.nih.gov/funding/transparency_in_reporting_guidance.pdf

Part 1B: Summary of Research Question *(Can be included on 1 additional page from Part 1A.)*

In addition, please address the following points (these need to be as bullet points on a separate page of your application):

Please be specific and concise. For the primary goal, do not state “establish safety.” It is well known that most safety outcomes occur relatively infrequently and small sample size studies will not reduce uncertainty about these. If establishing safety is a goal, “establish that the symptomatic intracerebral hemorrhage rate is not likely to be greater than 20%” would be responsive. Please see example hypothetical answers below.

1. Please indicate the target condition:

2. Please indicate the specific phenotype, if applicable:

3a. Please state in one sentence what the main goal of the current clinical trial or study will be:

3b. Please describe the biological rationale (and relevant preclinical evidence) for the study concept:

4. Please state the primary clinical endpoint:

5. Please estimate the general scale of the sample size you believe is needed (range is preferred):

6. If this study is successful, what would the next study look like:

7. Please state how findings from this line of work would change practice:

8. If applying to biomarker track, please describe the biomarker and how it would interact with the treatment or inform a clinical trial design:

Hypothetical Answers (using TBI as an example):

1. Traumatic brain injury
2. Comatose patients without space occupying extra-axial hemorrhage (such as epidural or subdural hematoma); parenchymal and subarachnoid hemorrhage included.
3. Two parts
    a. To determine if agent X reduces cerebral edema in acute TBI
    b. In a pig model of TBI with blinded outcome assessment, edema progression was reduced 20% when animals with controlled cortical impact were treated with agent X versus placebo (vehicle).
4. Cerebral edema at day 7 measured quantitatively using ADC mapping on MRI
5. 20-50 patients
6. Reducing post TBI cerebral edema would demonstrate proof of concept for agent X. This would provide motivation for a larger clinical study to establish dosing, schedule, and inclusion criteria. If agent X is shown to reduce TBI associated cerebral edema and reduce neurological disability, we would start using it to improve health.
7. We plan to develop companion biomarker Z, and will determine how well the longitudinal dynamics of this biomarker track imaging evidence of brain edema (quantitative ADC on MRI); this approach was promising in an animal study.

Part 2: Potential Funding Sources *(Limit 1 page)*

The second most highly weighted criterion is the review committee's estimated likelihood that the clinical trial that you are designing will actually enroll patients. Projects that use existing resources (e.g. study coordinators from local infrastructure, PI protected time for research, etc.) will receive the highest priority for participation in this course. In the template provided, please describe a specific, potential area(s) of funding to conduct the clinical trial protocol which you develop as part of the course, as well as a projected timeline with estimated dates for your application to be submitted. Include web links to funding announcements. Discuss why your potential project might be desirable to the funder. Examples of specific funding sources for early phase trials include: Local pilot mechanisms through CTSAs, foundations; NINDS or other NIH ICs – find relevant PARs that accept early clinical trials, or American Heart Association Fellow to Faculty award. For multi-center trials, please review the funding announcement to ensure your design would be within scope. You should review funding histories or

NIHRePORTER to assess whether clinical trials in this area are ongoing or within funding priorities of these potential sources.

Part 3: Team Members *(Limit 1 page)*
List the members of your team (mentor, coordinator, biostatistician, data management, engineer, etc.) include their role in your proposed project, expertise, and email. These members will be invited to your small group meetings (their attendance is not required). Provide a brief paragraph summarizing how you will organize and interact with the team.

Part 4a: Your Biosketches *(Limit 5 pages each)*
Please follow the instructions for the NIH biosketch format and append into your application: https://grants.nih.gov/grants/forms/biosketch.htm
Please ensure that you have edited your personal statement to address your motivation for taking, delineate previous clinical research experience, and how you think this course will help your future career.

Part 4b: Mentor Biosketch *(No page limit)*
The third most highly weighted criterion for selection is a dedicated mentor at your home institution that can help facilitate your success leading the project. The mentor's personal statement should describe the mentorship plan (how the mentor will help you implement the project). ***IMPORTANT:*** Please make certain you have a mentor that can devote time and attention to support you through the course.

Part 5: Department Chair's Letter *(Limit 2 pages)*

- Describe the applicant's research training, experience, and potential for a successful clinical research career;
- Outline the applicant's current competing responsibilities and availability of protected research time for the two years after the clinical trials course;
- For clinician applicants: Describe the resources that are currently available (contingent on IRB approval) for the applicant to conduct a clinical trial (study coordinators, project management, data management, lab processing, etc.)

Part 6: Other materials *(Limit 1 page)*
If you plan to seek the use of an investigational compound or device you MUST provide in writing evidence of the availability of that compound or device to you for this potential clinical trial.

Additional Information

Common Pitfalls to Avoid for CTMC Application:

- Unrealistic study in scale or translation of science
- Underpowered efficacy studies
- Lack of availability of drug and/or technology to be utilized, and uncertainty that it is practical and safe for humans
- No clinical trials are allowed in NINDS R21 planning grants. Should also consider Clinical and Translational Science Awards (CTSA) and Advocacy-funded research grants to obtain pilot data
- Implementation studies without patient centered outcomes
- It is not clear that the applicant is the scientific leader of their project (e.g., residents or fellows). See FAQ for more information.

Biomarker Studies

Clinical trials looking at biomarkers will be considered. “Biomarker” is defined by this course as a measurable quantity, previously identified and specific to the individual patient at a specific time. Biomarkers may be useful: (1) to predict the response, i.e., differentiate responders from non-responders, to a particular treatment strategy; (2) to differentiate patients with better from those with poorer outcomes, independently of a particular treatment; or (3) to demonstrate the proximal effect of a treatment, i.e., as proof of a proposed mechanism of action for an investigational treatment strategy. In the last case, the biomarker is not being fully qualified as a surrogate for the patient-centered outcome of interest but, instead, is being used to demonstrate that the treatment at least has a proposed proximate effect that is likely to be related to the desired clinical effect. Any application that is submitted for consideration in this pathway should clarify the intended use of the biomarker as above and include supporting references related to the proposed biomarker to be used. Applications proposing a single biomarker that is identified a priori will be considered. Studies intended to search for new biomarkers will NOT be considered.

Multi-Center Trials

Proposals for large multi-center trials will be considered. The multi-center proposals should ideally be aligned with the focus areas of one of the established NINDS clinical research networks. If someone is considering another network, please reach out to ctmc-info@umich.edu.

Application Template

Part 1A: Statement of Scientific Area and Key Information ***(Limit 1 page including references)***

Part 1B: Summary of Research Question ***(Can be included on 1 additional page from Part 1A.)***

1. Please indicate the target condition:

2. Please indicate the specific phenotype, if applicable:

3a. Please state in one sentence what the main goal of the current clinical trial or study will be:

3b. Please describe the biological rationale (and relevant preclinical evidence) for the study concept:

4. Please state the primary clinical endpoint:

5. Please estimate the general scale of the sample size you believe is needed (range is preferred):

6. If this study is successful, what would the next study look like, and/or please state how findings from this line of work would change practice:

7. If a biomarker study, please describe the biomarker and how it would interact with the treatment or inform a clinical trial design:

Part 2: Potential Funding Sources ***(Limit 1 page)***

Part 3: Team Members ***(Limit 1 page)***

Part 4a: Your Biosketches ***(Limit 5 pages each)***

Part 4b: Mentor Biosketch ***(No page limit)***

Part 5: Chair's Letter - Department Chair ***(Limit 2 pages)***

Part 6: Other materials ***(Limit 1 page)***