# 2022 Application Instructions

## Informational Webinar - January 21st, 2022 at 12p EST:

Join the course directors for an informational webinar with Q&A to learn more about the CTMC. This is a great opportunity to meet some of the course directors and faculty, get all your questions answered, and get a better understanding if the Course is a good fit for you and your professional goals. (If you are unable to attend the webinar recording will be posted to the CTMC website). The meeting information is below.

Join from a PC, Mac, iPad, iPhone or Android device:
Please click this URL to join. https://umich.zoom.us/j/99267039437

Or join by phone:
Dial(for higher quality, dial a number based on your current location):
US: +1 312 626 6799 or +1 646 876 9923 or +1 301 715 8592 or +1 346 248 7799 or +1 669 900 6833 or +1 253 215 8782
Canada: +1 438 809 7799 or +1 587 328 1099 or +1 647 374 4685 or +1 647 558 0588 or +1 778 907 2071 or +1 204 272 7920
Webinar ID: 992 6703 9437
International numbers available: https://umich.zoom.us/u/adehffnvU8

## Before applying you must agree to the following:

**This course requires:**

- **An ongoing time commitment from you, and**
- **Ongoing support from your mentor/supervisor**.

***Spring/Summer:*** You will be assigned to a small group that will start meeting in mid-late April; the frequency of meetings is approximately every two weeks with expected deliverables for each meeting. In addition, **attendance at the Residential Course (July 18-21, 2022 in Iowa City, IA) 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.

***Fall:*** The small groups will meet for several additional sessions in the Fall to help you finalize your protocol and proposal. You will be expected to give a presentation with a status update. There will also be opportunities to participate in a mock IRB and/or mock study section depending on how far along you are.

## 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.

**If you were in the 2021 cohort, please click here for more instructions.**

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**Applications are due by midnight February 28, 2022*.**
*Meritorious applications received prior to January 31, 2022 may be eligible for early acceptance.

**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. The ideal applicant typically is developing an **early phase** clinical trial, meant to answer key questions that would inform the design of a practice changing trial. We do consider biomarker-based studies, see additional information at the end of the instructions.

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.

## 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). The best designs for this course will seek to confirm important pre-clinical estimations of dose, mechanism, or target acquisition. The goal is to learn whether and how a follow up trial should be conducted. 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.
7. If agent X is shown to reduce TBI associated cerebral edema and reduce neurological disability, we would start using it to improve health.
8. 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 text box provided, please describe at least three specific, potential areas of funding to conduct the clinical trial protocol which you develop as part of the R25 course. Include web links to funding announcements as appropriate. Discuss why your potential project might be desirable to the funder. Examples of specific funding sources 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. You should review funding histories or NIH projectreporter to assess whether clinical trials in this area are ongoing or within funding priorities of these potential sources. List

**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 this course.

**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 the project's success. The mentor 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: Chair's Letter - Department Chair or Division Chief *(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 you MUST provide in writing evidence of the availability of that compound to you for this potential clinical trial.

# Additional Information

## Common Pitfalls to Avoid for CTMC Application:

- Too ambitious of a study in scale or translation of science
- Underpowered efficacy studies
- Need to ensure availability of drug and/or technology to be utilized, and make certain 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
- 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.

# 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:

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

8. 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 or Division Chief** ***(Limit 2 pages)***

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

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