

Name:
Institution:

Email:

CTMC Application Form 2019

Preliminary Application Instructions:

Please Check Back At Our Website <http://neurotrials.training> For Final Version To Be Released December 15, 2018.

Please review the website and consult the frequently asked questions. Please contact us (using information on website) with any questions not addressed there. Please note this course requires an ongoing time commitment. Starting in approximately late April, your small group will meet about every two weeks, and you will have expected deliverables for each session. In addition, the residential course is required and we will be expecting additional progress and preparation so that you can make the most progress there. Finally, the small groups will meet for several additional sessions to help you finalize your protocol and proposal in the fall.

You should submit your application at the following portal:

https://umichumhs.qualtrics.com/jfe/form/SV_er2LmGVF2Ejh2Bf

There are three potential pathways for applicants.

- Pathway A: Foundations Clinician – For applicants from a clinical discipline who are designing a clinical trial. We define a clinical trial as a research project that delivers some intervention (drug, device, diagnostic, behavioral) to patients in a prospective way.
- Pathway B: Foundations Biostatisticians – For applicants from biostatistics interested in developing skills in the design of clinical trials in neurological disease and injury. Those applying to this pathway do NOT need to have a partner from pathway A.
- Pathway E: Biomarker Clinician, the term “biomarker” refers to a measurable quantity, specific to the individual patient usually at a specific time, that is potentially of value: (1) to predict the response, i.e., differentiate responders from non-responders, to a particular treatment strategy; (2) to prognosticate more generally, i.e., 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.

Please note: participation in the small groups and attendance at the in-person residential course in Iowa City – July 22 – 25, 2019 is required for all accepted applicants. **Applications are due by midnight February 28, 2019.** Meritorious applications received earlier may be eligible for early acceptance (if received prior to January 31, 2019).

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Applicants should prepare all documents and combine into a **single PDF** that will be uploaded at the above [link](#).

Required Items for Application Form

Pathway	Parts 1 and 2: Science and potential funding	Part 3: Your biosketch	Part 4: Mentor biosketch(es)	Part 5: Chair's letter
A and E: Foundations Clinician or Biomarker Clinician	Yes	Yes	Yes	Yes
B: Foundations Biostatisticians	No	Yes	No	Yes

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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.

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 some 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. Please consider the NINDS Transparency in Reporting Guidelines when drafting this section and discuss the scientific premise underlying your idea.

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 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. Please state what findings in the current study would motivate you and the scientific community to move forward with additional research in this concept:
7. Please state how findings from this line of work would ultimately 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

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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 CTAs, 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 project reporter to assess whether clinical trials in this area are ongoing or within funding priorities of these potential sources.

Part 3: Your Biosketches (Limit 5 pages each)

Please follow the instructions for the 2015 NIH biosketch format and append into your application.

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-032.html> Please ensure that you have edited your personal statement to address your motivation for taking this course.

Part 4: Mentor Biosketches

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 and who will help them implement the project.

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 are currently available (contingent on IRB approval) for the applicant to conduct a clinical trial (study coordinators, project management, data management, lab processing, etc.)
- For biostatistician applicants to advanced track: Describe the release time the applicant will have available to conduct simulations and attend planning sessions in the Spring and Fall before and after the residential course.

Part 6: Other materials

If you plan to seek use of an investigational compound – evidence of the availability of that compound to you, for this potential clinical trial should be provided in writing.