Section 1. Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	National Institute of Neurological Disorders and Stroke (NINDS)
Research Opportunity Title	**NeuroNEXT Clinical Trials: Stage 2 Protocol Application (OT2)**
Activity Code	OT2: Other Transactions
Research Opportunity Number	OTA-24-014
Related Notices	OTA-24-013 (Stage 1)
Key Dates:	Posted Date: April 5, 2024
	Open Date (Earliest Submission Date): June 5, 2024
	Application Due Date(s): Rolling submission
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Section 2. Objectives of this Opportunity

The purpose of this research opportunity announcement (ROA) is to invite applicants to submit Stage 2 Protocol Applications for exploratory clinical trials or biomarker studies focused on neurological diseases to be conducted within the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT).

Background:

To facilitate the cooperation and partnering of public and private funding organizations, universities, academic medical centers, research institutes, contract research organizations, biotechnology companies, and pharmaceutical companies, NINDS has formed the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT: NINDS NeuroNEXT). NeuroNEXT has a Clinical Coordinating Center (CCC), a Data Coordinating Center (DCC) and multiple clinical sites that are geographically distributed across the United States.

This clinical research network develops and conducts multiple, scientifically sound, possibly biomarker-informed exploratory clinical trials evaluating the most promising therapies, whether from academic, foundation, or industry discoveries. Examples include phase 2 clinical trials and clinical research studies aimed at validating biomarkers and clinical outcomes in preparation for clinical trials, phase 2-3 trials if warranted by the nature of the studied population (such as rare diseases), and platform trials where applicable. The network is not specific to one disease; it has the capacity to coordinate a cadre of specialist investigators to implement studies efficiently in response to disease-specific opportunities. The network supports clinical research in both pediatric and adult populations.

The network is designed to increase the efficiency of clinical trials, to facilitate patient recruitment and retention, to increase the quality of neuroscience clinical trials, and to enable public-private partnerships.

To foster the development of clinical trialists, the NeuroNEXT investigators who have been selected for their experience and training in neurological clinical research provide a source of strong mentorship and support to investigators who are early in their career as approved studies are implemented within the infrastructure.

Objectives:

NeuroNEXT clinical trial applications are accepted and reviewed in a two-stage process. Stage 1 Preliminary Applications may be submitted by academic investigators, industry applicants, private institutions, or nonprofits (see Related Notices for the Companion ROA).

Stage 2 Protocol Applications are accepted by invitation only and involve the submission of more detailed information on the proposed clinical trial(s) and related activities. At Stage 2, the NeuroNEXT CCC is the applicant of record and may propose Multiple Principal Investigators (MPIs). The NeuroNEXT CCC will work with the Stage 1 applicants to obtain relevant information. Please refer to Section 5: Application Information and Submission for detailed information.

Under this ROA, the NINDS accepts Stage 2 Protocol Applications for clinical trials, biomarker validation studies, or proof of mechanism clinical studies to be conducted within NeuroNEXT. Applications for drugs or biologics should provide compelling scientific evidence that the investigational agent proposed for study will reach/act upon the designated target or that its mechanism of action is such that it is expected to be of benefit in ameliorating a specific aspect of the disease. Neurologic diseases chosen for study must fall within the primary responsibility of NINDS (www.ninds.nih.gov/funding/areas/index.htm).

Scope:

NeuroNEXT provides a robust, standardized, and accessible infrastructure to facilitate the rapid development and implementation of protocols in neurological disorders, in both adult and

pediatric populations. Examples of studies appropriate for the NeuroNEXT include, but are not limited to, those designed to:

- Evaluate and optimize the dose, formulation, safety, tolerability, or pharmacokinetics of an intervention in the target population.
- Select or rank the best of two or more potential interventions or dosing regimens to be evaluated in a subsequent trial, based on tolerability, safety data, biological activity, or preliminary clinical efficacy (e.g., futility trials).
- Validate biomarkers that are fit-for-purpose and can be used in future clinical trials.
- Evaluate biological activity relative to clinical endpoints.
- For medical devices, in addition to providing initial clinical safety data, appropriate studies are those that inform the next phase of development, usually by finalizing the device design, establishing operator technique, and/or finalizing the choice of study endpoints for the design of a pivotal clinical trial.

This ROA is not intended to support the conduct of a clinical trial where the primary aim is to confirm efficacy of a drug or biologic unless warranted by the nature of the studied population (such as rare diseases).

Applications in rare diseases are encouraged, while recognizing that available patient pools may not be adequate to meet the sample size requirements normally required to establish the efficacy of an intervention. NINDS acknowledges that innovative, non-traditional trial designs including adaptive designs may be appropriate, especially in rare disease studies. While NeuroNEXT is primarily intended for exploratory trials, the network will consider phase 2/3 trials in rare diseases.

The proposed asset must have completed first-in-human studies and have preliminary information on safety in humans and sufficient data to inform dose selection for a phase 2 clinical trial.

If the intervention is a drug, biologic, or device, an open IND (Investigational New Drug)/IDE (Investigational Device Exemption) is a funding milestone. Applicants must provide documentation from the FDA as per below:

- If open IND/IDE is submitted, applicants must provide documentation from FDA indicating “may proceed” or full approval.
- If IND/IDE is on full or partial hold or conditionally approved, applicants should discuss how they will address the issues/conditions and when they believe they will have FDA approval to proceed.
- If IND/IDE exempt (or does not require approval because determined nonsignificant risk), applicants must provide exemption letter or risk determination letter from FDA.

For Biomarker Validation Studies, biomarkers are defined as a characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. Categories of biomarkers include: susceptibility/risk, diagnostic, monitoring, prognostic, predictive, pharmacodynamic/response, and safety. Biomarker studies should define their intended Context of Use (a statement that fully and clearly describes the way the biomarker will be used in future clinical trials).

A separate clinical trials network has been established and funded by NINDS to conduct clinical trials and biomarker studies for stroke treatment, prevention and recovery; thus, NeuroNEXT

has been established for the conduct of studies in neurological disorders other than stroke. Multi-site studies in stroke prevention, treatment and/or recovery are not appropriate for this ROA; those studies would be considered by NIH StrokeNet: http://www.nihstrokenet.org/. Separate clinical trial networks also exist for the conduct of studies in neurological emergencies (SIREN: https://siren.network/) and pain (EPPIC-NET: https://www.ninds.nih.gov/Current-Research/Trans-Agency-Activities/NINDS-Role-HEAL-Initiative/NINDS-Role-HEAL-Initiative-EPPIC). Studies on these topics should be directed to the dedicated networks.

Studies primarily focused on biomarker validation may also apply to one of the NINDS Biomarker funding opportunities https://www.ninds.nih.gov/Current-Research/Focus-Tools-Topics/Biomarkers.

Phase 1 clinical trials should be directed to the exploratory clinical trial NOFO (PAR-22-142 and PAR-21-266). Phase 1b/2a trials requiring multi-center implementation can be considered under this ROA.

NIH Resources
As appropriate, applicants are encouraged to make use of the following resources for clinical research including:

(a) Clinical and Translational Science Award (CTSA) program)
(b) NeuroQOL
(c) NIH Toolbox
(d) PROMIS
(e) NINDS Common Data Elements

Potential applicants are STRONGLY encouraged to contact the NeuroNEXT Program Staff to discuss the application and application process prior to submission.

Section 3. Potential Award Information

NIH funds to conduct the study will be awarded to the NeuroNEXT CCC only after successful completion of both stages of application and review. The NeuroNEXT CCC then administers the funds to other NeuroNEXT research components or non-network entities (e.g., sites, contractors) as appropriate.

Authority:

This Research Opportunity Announcement (ROA) is issued with the goal of soliciting neurotherapeutics with an active IND or biomarkers for NeuroNEXT clinical trials. An Other Transaction (OT) Agreement will be used to fund clinical studies conducted within NeuroNEXT, pursuant to the OT authority described in section 402(n) of the Public Health Service Act, 42 U. S. C. 282(n).

Section 4. Eligibility

Organizations:

The following entity is eligible to apply under this ROA if selected after the NeuroNEXT Stage 1 application review: NeuroNEXT CCC.

Eligible Individuals (Program Director/Principal Investigator):

Any individual(s) identified by NeuroNEXT CCC as having the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s). The NeuroNEXT CCC may propose Multiple Principal Investigators (MPIs). Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

Section 5. Application Information and Submission

Application Process Overview:

The NeuroNEXT program uses a two-stage application and review process.

Stage 1 Preliminary Application: The asset holder will submit a Stage 1 Preliminary Application under the Stage 1 ROA (see Related Notices for the Companion ROA), including all required documents. This application must include detailed information on the proposed asset, including prior basic, pre-clinical and clinical research completed and rationale as well as brief information on the proposed study population and design. Stage 1 Preliminary Applications are received and reviewed on a rolling basis. The review includes an independent /objective review by a panel of external experts convened by the NINDS. No funding is provided at Stage 1.

Stage 2 Protocol Application: Upon completion of the Stage 1 review process, the applicant may be invited to work with the NeuroNEXT to develop a full clinical protocol (including budget and timeline) for submission under this ROA, resulting in a Stage 2 Protocol Application. The NeuroNEXT CCC will be responsible for submission of the Stage 2 application package and may propose MPIs. The following will be considered in making funding decisions: 1) Scientific and technical merit of the proposed project as determined by scientific independent and objective review, 2) Availability of funds, and 3) Relevance of the proposed project to program priorities. Protocols selected following the review will be presented to the National Advisory Neurological Disorders and Stroke (NANDS) Council. Following review by the NANDS Council, a funding decision will be made by the NINDS Director. If funded, OT trial funds will be awarded to the NeuroNEXT CCC and study implementation within the NeuroNEXT may begin.

NeuroNEXT Stage 2 Protocol Application Information:

Application Requirements:

Complete applications must be submitted by the Recipient Business Official/Signing Official. The organization must be registered in eRA Commons with one person designated as the Principal Investigator (PI) and one person designated as the Signing Official (SO). The SO's signature certifies that the applicant has the ability to provide appropriate administrative and scientific oversight of the project and agrees to be fully accountable for the appropriate use of any funds awarded and for the performance of the OT award-supported project or activities resulting from the application.

The application must clearly and fully demonstrate the applicant's capabilities, knowledge, and experience and the budget proposed. Full applications must be submitted in text-recognizable PDF (Adobe) format and must include the following information.

1. **Cover Page, Abstract, and Specific Aims**: Applicants for NIH Other Transactions shall include a cover page, an abstract, and specific aims in each application. Abstracts are limited to one page, and specific aims are limited to three pages.

The Cover Page should include (no more than 1 page)

- Number and title of this ROA
- Project title
- The Recipient's
    - Legal entity name
    - Address and contact information
    - Unique Entity ID# and expiration date
    - EIN number
- Principal Investigator(s) first and last name, title, organization, mailing address, email address and phone number (with NIH Commons Account information). If multiple PIs are named, the Contact PI must be clearly identified.
- Key personnel: first and last name, title, organization, mailing address, email address and phone number.
- The name and contact information for the Recipient's Business official, the person authorized to negotiate and bind the Recipient as a signatory to Other Transactions Agreement.
- The total cost proposed.

Abstract ("Abstract.pdf"; no more than 1 page): The project abstract is a succinct and accurate description of the proposed work and should be able to stand on its own (separate from the application). It should be informative to other persons working in the same or related fields and understandable to a scientifically literate reader. Do not include proprietary, confidential information or trade secrets in the abstract. If the application is funded, the project abstract will be entered into an NIH database and made available on the NIH Research Portfolio Online Reporting Tool (RePORT) and will become public information. The attachment is limited to one page.

Specific Aims ("SpecificAims.pdf"; no more than 3 pages): State concisely the goals of the proposed research and summarize the expected outcome(s), including the impact that the results of the research will have on the research field(s) involved. List succinctly the specific objectives of the research. This attachment is limited to three pages.

2. **Clinical Trial Protocol Application:** The Clinical Trial Protocol Application should include following information:

    - Clinical Trial Protocol- The NIH-FDA Phase 2 and 3 IND/IDE Clinical Trial Protocol Template) (NOT-OD-17-064) shall be used as a guideline for the protocol. That template must be adapted to reflect the asset and population to be studied.
    - Go/No-Go criteria for the next stage of clinical development and a brief description of the potential future study.
    - A detailed Timeline and Milestones
    - Statistical analysis plan
    - A list of protocol Investigator(s) and key research personnel
    - Facilities and other resources
    - A detailed Budget and budget justification as further explained below

3. **NIH Biosketches:** Biosketches of each key personnel must be included (no more than five (5) pages in length). NIH biosketches must conform to a standardized format.

4. **Multiple Principal Investigators:** Applications that involve more than one PD/PI must include a Leadership Plan that describes the roles, responsibilities, and working relationships of the identified PD/PIs.

5. **Letter of Support:** If collaborations have been established, include letters of collaboration in the application that document the role of each collaborator. Letters should be combined into a single PDF. Applicants should include a consolidated list of names of providers of letters of support.

6. **Budget Information**: The budget should be largely planned on a fee-for-service basis with detailed per-patient costs. That budget may include clinical trial costs such as:

   Up to 4 person months for the protocol PD(s)/PI(s) (even if that person is also a NeuroNEXT site PD(s)/PI(s)).

   - Up to 3 person months of support for a study-specific clinical coordinator at the applicant's site if the NIH-funded site coordinator is at capacity with NeuroNEXT trials or does not have necessary expertise to assist with the proposed study. If the applicant is not at a NeuroNEXT clinical site, up to 12 person months support for a study-specific clinical coordinator may be included.
   - Study-related procedures/materials.
   - Clinical site operations for any ad hoc sites which are proposed.

   The budget will not include costs that are already covered by the NINDS infrastructure:

   - NeuroNEXT site PD(s)/PI(s) time other than the protocol PD(s)/PI(s)
   - NeuroNEXT site coordinator time.

   NINDS expects that the total cost for the proposed project (direct cost plus F&A) will not exceed $25,000 per subject randomized into the trial. Budgets exceeding this guideline should be adequately justified in the application. The NINDS strongly encourages applicants to consider simple and/or pragmatic trial designs that minimize per-subject data collection and cost.

   The budget shall contain sufficient information to allow the Government to perform a basic analysis of the proposed cost of the work. This information shall include the amounts of the line items of the proposed cost. These elements will include the following elements by milestone event and/or proposed period as applicable:

   - Direct Labor – Individual labor category or person, with associated labor hours and unburdened direct labor rates;

   - Indirect Costs – Fringe Benefits, F&A, etc. (must show base amount and rate). Offerors must submit a copy of their most recent indirect cost rate agreement negotiated with any federal audit agency, if applicable;

   - Travel – Separate by destinations and include rationale for travel, number of trips, durations - number of days, number of travelers, per diem (hotel and meals in accordance with the Federal Travel Regulations), airfare, car rental, if additional miscellaneous expense is included, list description and estimated amount, etc.;

- Subawardee – A separate detailed budget shall be submitted by each proposed subawardee. The subawardee's proposal shall include on company letterhead the following:

    - Complete company name and mailing address, technical and administrative/business point of contacts, email address, and telephone number.

    - Include the Unique Entity ID .

    - A commitment letter from the proposed subcontractor's business official that includes:

        - Willingness to perform as a subawardee for specific duties (list duties) or a SOW;

        - Proposed period of performance;

        - Supporting documentation for proposed costs (personnel documents to verify salaries, vendor quotes for equipment, negotiated indirect cost rate agreement)

- Consultants – For proposed consultants, provide draft consulting agreement or other document which verifies the proposed loaded daily/hourly rate and labor category;

    - Written verification from the consultant of their proposed rate, along with a statement that it is their usual and customary rate charged to other customers;

    - Description of the work to be performed by the consultant and direct relevance to the work. Include information on why this expertise is not available in-house

- Materials & Supplies – Should be specifically itemized with costs or estimated costs. Where the total cost is greater than $3,500, indicate pricing method (e.g., competition, historical costs, market survey, etc.). Include supporting documentation, i.e., vendor quotes, catalog price lists, and past invoices of similar purchases.

- Other Direct Costs – Especially any proposed items of equipment. Equipment generally must be furnished by the Offeror. Justifications must be provided when Government funding for such items is sought.

<u>Salary Rate Limitation:</u>

- Pursuant to current and applicable prior NIH appropriations acts, it is anticipated that Offerors submitting applications under this ROA will be subject to a salary rate limitation on funds used to pay the direct salary of individuals.

- Congress has stipulated in NIH appropriations act that, under applicable extramural awards appropriated funds cannot be used to pay the direct salary of an individual at a rate in excess of the Federal Executive Schedule Level II.

- For purposes of the salary rate limitation, the terms “direct salary,” “salary,” and “institutional base salary,” have the same meaning and are collectively referred to as “direct salary”, in this clause. An individual's direct salary is the annual compensation that the Offeror pays for an individual's direct effort (costs) under the award. Direct salary also excludes fringe benefits, overhead, and G&A expenses (also referred to as indirect costs or facilities and administrative [F&A] costs). Note: The salary rate limitation does not restrict the salary that an organization may pay an individual working under an NIH award; it merely limits the portion of that salary that may be paid with Federal funds.

- The salary rate limitation also applies to individuals under subawards.

- See the salaries and wages pay tables on the U.S. Office of Personnel Management Web site for Federal Executive Schedule salary levels that apply to the current and prior periods.

7. **Data Management and Sharing Plan (no more than 2 pages):** In accordance with NIH Policy for Data Management and Sharing, describe how the proposed data generated from the project will be managed and shared. For elements to include in the Data Management and Sharing Plan, please see Data Management & Sharing Policy Overview, Writing a Data Management & Sharing Plan | Data Sharing (nih.gov) and NOT-OD-21-014 , NOT-OD-23-053: Supplemental Information to the NIH Policy for Data Management and Sharing: Elements of an NIH Data Management and Sharing Plan. NIH respects and recognizes Tribal sovereignty and American Indian and Alaska Native (AI/AN) communities’ data sharing concerns. For research teams working with Tribes and AI/AN communities, please refer to NOT-OD-22-214: Supplemental Information to the NIH Policy for Data Management and Sharing: Responsible Management and Sharing of American Indian/Alaska Native Participant Data.

8. **Use of Common Data Elements in NIH-funded Research**: Many NIH ICs encourage the use of common data elements (CDEs) in basic, clinical, and applied research, patient registries, and other human subject research to facilitate broader and more effective use of data and advance research across studies. CDEs are data elements that have been identified and defined for use in multiple data sets across different studies. Use of CDEs can facilitate data sharing and standardization to improve data quality and enable data integration from multiple studies and sources, including electronic health records. NINDS has identified CDEs for many clinical neurological/neuromuscular diseases and types of outcomes (e.g., patient-reported outcomes). NINDS provides resources for CDEs (https://www.commondataelements.ninds.nih.gov/#page=Default) to assist investigators in developing protocols, case report forms, and other instruments for data collection. Investigators are encouraged to consult the NINDS CDE website and describe in their applications any use they will make of these CDEs in their projects.

Submission Information:

Applications to the **NeuroNEXT Clinical Trials: Stage 2 Protocol Application (OT2)** may be submitted after the first receipt date shown under the “Key Dates” section of this announcement. Applications are submitted via eRA ASSIST. Use this ROA number when submitting the application. Detailed instructions for submitting OT Applications can be found at ASSIST-Instruction-Guide-for-NIH-Other-Transactions.docx (live.com). Complete the Human Subjects

and Clinical Trials Information (HSCT) form in ASSIST according to the User Guide: https://www.era.nih.gov/files/ASSIST_user_guide.pdf

Upon receipt, applications are evaluated by NINDS for completeness, compliance with application requirements, and responsiveness. Applications that are incomplete, non-compliant, and/or nonresponsive will not be reviewed and the applicant will be so notified.

Applications not responsive to this ROA:

Nonresponsive applications include those that involve any of the following examples:

- Nonclinical studies of disease mechanism or therapeutic mechanism of action studies
- Animal studies
- Single site studies
- Research focused entirely on natural history studies

Section 6. Independent/Objective Review Information

Stage 2 Protocol Applications will undergo objective, independent review. Independent review is an assessment of scientific or technical merit of applications by individuals with appropriate scientific knowledge and expertise. Conflicts-of-interest of review panel members are appropriately managed during the review process in accordance with standard NIH policies. Independent review provides information essential to ensuring selection of meritorious applications that best meet the needs of the program using the criteria delineated below and ensures that application selection is conducted in a fair, objective manner free of prejudices and biases. The Independent reviewers consider only the review criteria below in their individual assessment of scientific merit. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field, or a proposed clinical trial may include study design, methods, and intervention that are not by themselves innovative but address important questions or unmet needs. Additionally, the results of the clinical trial may indicate that further clinical development of the intervention is unwarranted or that it might lead to new avenues of scientific investigation.

Independent/Objective Review Criteria:

1. Significance/Innovation
    a. How will successful completion of this clinical trial change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?
    b. Does the clinical trial protocol include innovative elements, as appropriate, to advance scientific knowledge or clinical practice?
    c. Is the potential impact of the intervention/biomarker on the disease and patients clear? Would the project advance the field even if the trial is negative?
2. Approach
    a. Is the study design justified and appropriate to address primary and secondary outcome variable(s)/endpoints that will be clear, informative, and relevant to the hypothesis being tested? How appropriate are the primary and secondary outcome measures?

b. Are rigorous testing methodologies (e.g., biomarker assays) available and proposed to assess the safety and efficacy outcomes of the therapeutic candidate in the clinical trials?
c. Is the trial appropriately designed to conduct the research efficiently?
d. Are the study populations (size, gender, age, demographic group), proposed intervention arms/dose, and duration of the trial, appropriate and well justified?
e. How appropriate are the eligibility criteria, randomization/blinding methods (if applicable), and sample size?
f. Are the plans for recruitment outreach, enrollment, retention, handling dropouts, missed visits, and losses to follow-up appropriate to ensure robust data collection? Are the planned recruitment timelines feasible and is the plan to monitor accrual adequate?
g. Are planned analyses and statistical approach appropriate for the proposed study design and methods used to assign participants and deliver interventions? Is the study design adequately powered to answer the research question and provide interpretable results?
h. Does the protocol identify research-related risks and provide ways to minimize those risks?
i. Are the plans for quality control, quality assurance and quality monitoring adequate? Are the procedures for data management and quality control of data adequate at clinical site(s) or at center laboratories, as applicable?
j. Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?
k. Are the study timeline and milestones feasible?
l. Will the protocol provide data that will inform a subsequent go/no-go decision about whether to move the asset forward for further development and later phase clinical trials?

3. Expertise and Resources

a. Do the investigators have the relevant experience and expertise in the subject matter and clinical trial execution? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?
b. Are the institutional support, equipment, and other physical resources adequately available to the investigators for the project proposed?
c. Are the administrative, data coordinating, and laboratory/testing centers, appropriate for the trial proposed?
d. Does the application adequately address the capability and ability to conduct the trial at the proposed sites? Are the plans to add or drop enrollment sites, as needed, appropriate?
e. Does this project include a partnership with the private sector (e.g., patient groups and/or industry), and if so, have agreements with proposed partners been established?

f. Are substantive letters of support or other documentation provided to assure commitment of subcontractors, consultants, and/or service agreements for personnel and facilities?

Additional Review Criteria:

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing an overall impact score, but will not give separate scores for these items.

Study Timeline

1. Is the study timeline described in detail, taking into account start-up activities, the anticipated rate of enrollment, and planned follow-up assessment? Is it well-justified?
2. Does the project incorporate efficiencies and utilize existing resources (e.g., CTSAs, practice-based research networks, electronic medical records, administrative database, or patient registries) to increase the efficiency of participant enrollment and data collection, as appropriate?
3. Are potential challenges and corresponding solutions discussed (e.g., strategies that can be implemented in the event of enrollment shortfalls)?

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials. For additional information on review of the Human Subjects section, please refer to the Guidelines for Reviewers: Protections for Human Subjects Review Criterion

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research.

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Additional Review Considerations:

As applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not consider them in providing an overall impact score.

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans
Reviewers will comment on whether the following Resource Sharing Plan, or the rationale for not sharing the following types of resources (as applicable), are reasonable: Sharing Model Organisms.

Authentication of Key Biological and/or Chemical Resources
For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support
Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Composition of Objective Review Panel:

Application review is carried out by an established panel of experts with complementary knowledge in multiple areas related to the proposed study subject matter and the conduct of clinical trials such as pharmacokinetics, biostatistics, biological mechanisms, medical devices, pharmaceutical industry development, and other relevant scientific and clinical expertise. NIH program officials attend the review meetings to provide programmatic input. Summary statements of the review panel meetings will not be made available. However, feedback on the Independent/Objective Review and the NINDS decision on the application are provided to applicants. Appeals are not allowed.

Selection Process:

The NINDS will select applications based on their scientific and technical merit, including consideration of the issues identified during independent/objective review and relevance of the proposed project to program priorities for presentation to NANDS Council and approval by the NINDS Director before award of the Other Transactions funding and study implementation within the NeuroNEXT.