National Institute of Diabetes and Digestive and Kidney Diseases

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Evaluating Neurocognitive Complications of Pediatric Type 1 Diabetes (T1D) and Potential Risk and Protective Factors

RFA-DK-23-009: Evaluating Neurocognitive Complications of Pediatric Type 1 Diabetes (T1D) and Potential Risk and Protective Factors Biostatistics Research Center (U01 Clinical Trial Not Allowed) (nih.gov)

RFA-DK-23-010: Evaluating Neurocognitive Complications of Pediatric Type 1 Diabetes (T1D) and Potential Risk and Protective Factors Clinical Centers (U01 Clinical Trial Not Allowed) (nih.gov)

FREQUENTLY ASKED QUESTIONS:

Are PIs expected to partner with other clinical sites to propose a potential consortium prior to applying for this NOFO?

The goal of these Notices of Funding Opportunity (NOFOs) (RFA-DK-23-009; RFA-DK-23-010) is to ultimately create a clinical consortium that will enact an agreed-upon common protocol. It is intended that each potential clinical site will submit its own application for the clinical center RFA (RFA-DK-23-010) and each potential biostatistics research center (BRC) will submit its own application for the BRC RFA (RFA-DK-23-009). The applicants/sites selected for funding will then become the new consortium and the Principal Investigators (PIs) from each selected application will populate the steering committee, along with a project scientist from NIDDK and a community engagement representative. The steering committee will then design a core common protocol to be adopted by each site.

If selected, will a clinical center's proposed protocol be adopted by the consortium, as is?

No. The steering committee (comprised of Principal Investigators from the funded clinical centers/BRC, NIDDK Project Scientist, and a community engagement representative) will ultimately design the core protocol to be carried out across all sites. This approach allows the study section to evaluate a hypothetical protocol submitted by a clinical center that is not binding but supports the clinical center team's expertise in this area.

Can an investigator be included on both a Biostatistics Research Center application and Clinical Center application?

While we certainly appreciate that many investigators have longstanding collaborations in this area, the NOFOs are written for each BRC or clinical center to individually compete. Investigators may be listed on multiple applications (e.g., an investigator could be listed as a Co-Investigator on a BRC application and Principal Investigator on a clinical center application). However, if both were funded, an investigator cannot hold a key personnel role on *both* the funded BRC and a funded clinical center—that would be a conflict since the BRC is responsible for the oversight of study conduct across the clinical centers.

Therefore, if an investigator is listed as key personnel on both a submitted BRC application and a submitted Clinical Center application, the applications should briefly address how the potential conflict will be handled if both applications are selected for funding.

How should Clinical Center applications incorporate costs that will be the responsibility of the Biostatistics Research Center when developing a budget?

Please read the budget details in RFA-DK-23-009 and RFA-DK-23-010 closely. Clinical Center applicants may assume that the cost of supplies related to cognitive and neuropsychological evaluation, CGM, and laboratory assays will be covered in the budget of the BRC. Clinical Centers will be responsible for costs associated with local conduct of the study, such as: neuroimaging assessments (e.g., scanner fees), consortium-related meeting travel, local facility fees, participant reimbursement, recruitment activities, and other site-specific operating costs. We anticipate that the clinical centers will make their best attempt to provide a reasonable budget for their site, with the understanding that the final protocol will inform the final budget at each site and the BRC.

Can a clinical trial be proposed for RFA-DK-23-010?

Clinical trials are not allowed, as the project is intended to be an observational study without clinical intervention or randomization of treatment. While the study will involve human participants and the evaluation of health-related biomedical and behavioral outcomes, participants will not prospectively be assigned to an intervention or evaluated based on the effect of an intervention, thus falling under the definition of a Clinical Study, as opposed to Clinical Trial. For more information on NIH's Clinical Trial definition, visit: https://grants.nih.gov/policy/clinical-trials/definition.htm

Should clinical center applicants base power calculations and budgets on their site's projected cohort or that of the consortium?

We anticipate that the clinical centers will make their best attempt to provide a reasonable budget for their site, with the understanding that the final protocol will inform the final budget at each site and the BRC. Clinical center applicants should provide sample size calculations for the entire study, but also clearly state the proposed enrollment targets for their specific site. The budget would then be based on the study being proposed at the applicants' local site.

Where can information be found on data management and sharing, including information on archiving data and biosamples at the NIDDK Central Repository?

Please refer to the NIDDK Central Repository website for the most up-to-date guidance: https://repository.niddk.nih.gov/home/.

What are the expected frequencies of reports provided by the BRC to the Steering Committee, NIDDK, the Observational Study Monitoring Board, and other entities? Can any guidance be given on the amount of effort to be budgeted to work on these reports?

Per the NOFO, the BRC will be expected to prepare appropriately detailed reports for the Steering Committee, the OSMB, and NIDDK staff at regular intervals. The frequency should be in accordance with

the proposed project's projected timeline and applicable milestones. Level of effort should be gauged based on the frequency/schedule proposed and phase of the study. Applicants should do their best to project these parameters, but ultimately, reporting guidance will be formalized by the Steering Committee.

Is it possible that the funding opportunity will be extended/renewed to increase the follow-up time for study participants?

The current funding period as listed on the NOFO is limited to 5 years.

Are non-U.S. investigators and/or entities allowed to apply to the RFAs?

Unfortunately, this opportunity is restricted to US/domestic components. This is due to the initiative's focus on characterizing multiple nuanced facets of this clinical population, including social determinants of health and health care system factors, which (as you know) can vary greatly across countries.

How will a comparison group be identified/selected for the study protocol?

As noted in the RFA, the proposed study should include pre-pubertal children newly diagnosed with type 1 diabetes and an appropriate comparison group. Applicants should identify the comparison group that they feel will best meet the proposed study objectives. It is expected that the Steering Committee will have the final say in identifying an appropriate comparison group during the design and development of the common study protocol.

Can research protocols propose evaluation of novel risk and/or protective factors not listed in the NOFO?

The risk and protective factors identified in the NOFOs are examples and not exhaustive. Investigators are encouraged to consider novel risk and protective factors for neurocognitive effects of T1D in children.

ADDITIONAL FAQs - *Added September 29, 2023*

Does a BRC need expertise in pediatric type 1 diabetes, given that this expertise will be represented at Clinical Centers and on the Steering Committee?

It is recommended that the BRC has the requisite knowledge and expertise to draft a strong application and provide oversight for the consortium (if funded). However, the BRC doesn't specifically need pediatric T1D expertise since there will be a steering committee with broader expertise.

Should Clinical Centers budget for biostatistical support, given that the Biostatistics Research Center (BRC) will be leading analyses?

It is recommended that the clinical center personnel represent the requisite knowledge and expertise to draft a strong application, including a proposed analysis plan, and provide oversight for data management and analytic support. Beyond that, it is expected that the Biostatistics Research Center (BRC) will provide the bulk of the biostatistical and analytic expertise throughout the funding period,

including conducting analyses and interpretation of primary study data in conjunction with the Clinical Centers.

For RFA-DK-23-009 (Biostatistics Research Center), is the Protection of Human Subjects section applicable?

Yes, as noted in RFA-DK-23-009, the Protection of Human Subjects section is applicable. For more information, please review the section of the RFA under **PHS Human Subjects and Clinical Trials Information**. Some aspects of information provided in the Protection of Human Subjects section will change/update based on the final study protocol determined by the Steering Committee; however, applicants need to do the best they can to provide information in each section and, as needed, explain in appropriate sections that the final study design/protocol will be determined by the Steering Committee.

Are foreign consultants allowed for RFA-DK-23-009 and/or RFA-DK-23-010?

No, as noted in the RFA, foreign components are prohibited.

For RFA-DK-23-009 (Biostatistics Research Center), are there any guidelines for how to budget for data management and sharing costs?

Per the latest Application Guide, "For applications submitted for due dates on or after October 5, 2023, DMS costs must be requested in the appropriate costs category," as opposed to the previous guidance to include personnel costs specific to DMS as a specific line item under Section F.8.-17 Other. Additional information on allowable DMS costs can be found at 8.2.3 Sharing Research Resources (nih.gov) and NIDDK's Data Management & Sharing website.

For specific information on the NIDDK Central Repository (NIDDK CR), please visit their website, https://repository.niddk.nih.gov/home/. As an NIDDK-funded project there should not be additional submission/management costs associated with archiving study data within the NIDDK CR; however, NIDDK CR can provide the most up-to-date information.

For RFA-DK-23-010 (Clinical Centers), how should the 1-year planning period be incorporated into the research strategy and study timeline?

Year 1 is a planning year, and this should be reflected in your research strategy and overall timeline (5-year project with the 1st year as a planning year). There is a different budget for Y1 as compared to Y2-5 to reflect the planning year, and, for the clinical centers (RFA-DK-23-010), budgets may not exceed $200,000 in direct costs for grant year 1 (planning year) and $400,000 in direct costs for each grant year 2 – 5.

For RFA-DK-23-010, is a longitudinal study design expected or is this consortium intended to be focused on recruitment and cross-sectional baseline assessments of participants?

For this RFA, a longitudinal study design is expected. Although the ultimate design of the study will be finalized by the Steering Committee, this is expected to be a longitudinal observational study with clinical centers recruiting a cohort of pre-pubertal youth recently diagnosed with type 1 diabetes and a

comparison sample and collecting data (as determined in the core study protocol agreed upon by the Steering Committee) at multiple timepoints.

Please reach out to the scientific contacts listed on the NOFOs - Dr. Maureen Monaghan Center (maureen.center@nih.gov) or Dr. Theresa Teslovich Woo (theresa.woo@nih.gov) - with questions related to this opportunity.