Request for Applications
2022-2023 Pilot/Feasibility Project Program (PFPP)

Key Dates:
Date of RFA: November 23, 2021
Submission Due: January 7, 2022
Award Announced by: February 7, 2022
Funding Begins: September 1, 2022
Funding Ends: August 31, 2023 (may apply for a 2nd year of funding)

Mission: The objective of the PHEFREE pilot/feasibility program is to provide funding for studies of innovative ideas or hypotheses which, if successful, could lead to improvement in the understanding, prevention, diagnosis and/or treatment of hyperphenylalaninemia, biopterin defects and related conditions.

Proposed pilot projects may include:
1. development of novel laboratory assays or clinical instruments (including evaluation of cognitive and emotional skill)
2. development of strategies for assessing current therapeutic interventions through biomarkers
3. conducting pilot clinical trial
4. performing supplemental testing/data mining in subpopulations of the longitudinal study or National PKU Alliance (NPKUA) registry to investigate outcomes, focusing on morbidities.

Pilot projects involving the use of animal models are not permitted by the parent RFA.

Pilot projects should generate feasibility data and have the potential to lead to future protocols or external grants for the diagnosis and treatment of subjects with hyperphenylalaninemia, biopterin defects and related conditions. Applicants are encouraged to collaborate with scientists across multiple PHEFREE sites or with scientists outside the PHEFREE community as appropriate to achieve these goals.

Any project meeting the NIH definition of a clinical trial must specifically explain how the proposed study design, sample size, statistical approach and planned analyses are appropriate for the project. Pilots proposing a clinical trial must also include provisions for rigorous data management, quality assurance, and safety monitoring. These monitoring activities are distinct from the requirement for study review and approval by an Institutional Review Board (IRB). For details about the Policy of the NIH for Data Safety Monitoring of Clinical Trials, see the PHS 398 Instructions (Rev. 03/2020 and related links). A general description of the data and safety monitoring plans should be included in the application. The NIH also requires that all investigators proposing research involving human subjects are educated on the protection of human research participants.
Mechanism: Funding will be provided for one year with the possibility of a second year of funding based on productivity and availability of funding. In this cycle (2022-2023), funding of up to $50,000 direct costs is available for support of one project. Indirect costs are allowed per the standard NIH rate agreement with the applicant’s institution. Pilot projects are encouraged to be collaborative among scientists in multiple PHEFREE sites, or with scientists outside the PHEFREE community. A maximum of one application can be submitted from each PHEFREE site/institution. Applications from non-PHEFREE sites will be considered, but must include at least one PHEFREE investigator as a collaborator. Funds may be used for salary support, technical support, and/or supplies. The budget submitted does not need to be approved and signed off by the applicant’s institution unless the project is selected for funding. The applicant whose project is selected for funding will be asked to submit an official budget at the time the project’s selection is announced. The selected project will need to obtain any necessary IRB approvals before funds can be released.

Application Process: M.D., Ph.D., and M.D./Ph.D. investigators are eligible to apply.

Please submit a complete application. The full application should be submitted through the RDCRN grants portal as a PDF document (11 pt. Arial font, half-inch margins) and transmitted by 11:59 PM EST on January 7, 2022.

The application must include the following elements:

- Project title
- Project summary (page limit, half page)
- Project relevance to the overall mission of PHEFREE explaining how trainee activities will be integrated not only into the training mission but also the scientific and clinical mission of the PHEFREE Consortium (page limit, one page)
- Detailed Budget including percent effort, salary, and fringe benefits
- Budget Justification
- NIH biosketch of the applicant (please format according to the standard format https://grants.nih.gov/grants/forms/biosketch.htm)
- Applicant’s other support
- If applicant is not a PHEFREE site PI, include a letter of recommendation/support from the sponsoring PHEFREE site PI (one-page limit)
- Research strategy with the following sections (6 page limit)
  - Specific aims (limit, one page)
  - Background, Significance, Innovation, and Approach
  - A timeline of proposed research activities
- Human Subjects Information (if applicable) that includes:
  - Protection of Human subjects (if applicable)
  - Recruitment and retention plan
  - Data Safety monitoring plan (if applicable)
  - Inclusion of women and minorities (if applicable)
  - Inclusion of children (if applicable)

REFERENCES (no page limit)

Review criteria: The “study section” for the applications will consist of a group of 3-5 PHEFREE site PIs
recruited by the Chair of the Pilot Project Selection Committee. The site PIs will recuse themselves if an application is from their institution. External Ad Hoc reviewers may be called as needed. NIH scale scores and related reviews will be anonymously given to each applicant after discussion of each application. The Chair of Pilot Project Selection Committee (Nicola Longo, MD, PhD) will forward mean scores and recommendation for funding to the PI of PHEFREE. Each applicant will be reviewed based on the following criteria:

- Does the application describe the plan for ensuring that the proposed project is related to hyperphenylalaninemia, biopterin defects and related conditions, promotes clinical trial readiness and has the potential to move the field forward?
- Does the application adequately address how the pilot/feasibility project leverages existing resources and infrastructure?
- Does the application adequately address pilot/feasibility project milestones and deliverables?
- Does the application adequately address how the pilot/feasibility projects will be evaluated and managed at the end of the first year?
- Quality of science - overall impact, innovation, significance and approach.

**Reporting and Sharing Outcomes:** Successful applicants are expected to publish results of data analysis projects/original projects and to present results to the PHEFREE Consortium at an in-person meeting or conference within a year of the grant funding period. Any research project that meets the NIH definition of a clinical trial will also be required to adhere to all NIH requirements for clinical trial registration and results reporting.

**Deadline for submission and funding dates:**
Deadline for submission is January 7, 2022. Awards will be announced by February 7, 2022. Funding will begin September 1, 2022. Any required IRB approvals need to be in place before funds can be released to the awardee.

The complete application should be submitted through the grants portal on the Rare Diseases Clinical Research Network (RDCRN) member website at https://grants.rarediseasesnetwork.org/grants/phepilot2022. Members can log in to apply with their RDCRN accounts. If you are not a member of the RDCRN, you will need to log in using one of the methods on the login page. Please contact Hadley Morotti if you need assistance.

Please contact Dr. Longo or Ms. Morotti with any questions you may have about the application process:

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