-RFA-HG-17-008
-RFA-HG-17-009
-RFA-HG-17-010

Frequently Asked Questions:

Can you describe the nature of a pragmatic clinical trial in more detail?

Prospective trials evaluating the validity and utility of genomic medicine interventions are needed for the implementation of genomics into clinical practice. Pragmatic clinical trials exist on a continuum with randomized clinical trials, where traditional randomized clinical trials are often designed to demonstrate efficacy under ideal conditions. Pragmatic clinical trials, however, are designed to assess effectiveness in routine settings. Pragmatic clinical trials are therefore better integrated with routine clinical care and are designed to produce practical evidence that can ultimately be used to improve practice and policy. IGNITE II applications should propose trials that focus on routine, "real world" settings that will ultimately be useful in assessing the impact of incorporating a genomic medicine intervention into clinical practice and if successful could be rapidly implemented in most clinical care settings.

Further discussion of pragmatic clinical trials can be found at Ford I, Pragmatic Trials.

Could previously enrolled patients with retrospectively collected data be included in the minimum sample size to be enrolled by a Clinical Group (CG)?

Each CG is expected to consent and enroll a minimum of 3,000 patients across all IGNITE II implemented protocols, and to complete screening and enrollment within a 12-month period of initiation of each protocol. While you can include patients previously enrolled in another clinical study, data for the pragmatic clinical trials should be collected prospectively.

How many diseases, patient groups, and geographic regions should my application include?

IGNITE II will assess approaches for real-world application of genomic medicine in diverse clinical settings. As stated, applicants to RFA-HG-17-008 are expected to recruit a minimum of 35% of patients who come from racial or ethnic minority populations, underserved populations, or populations who experience poorer medical outcomes. Applicants to the companion RFA HG-17-009 are expected to recruit a minimum of 75% of such patients. Applicants to both RFAs are expected to recruit 50% of patients from diverse clinical settings such as community hospitals, family medicine clinics, and primary care practices.

Beyond the minimum requirements, the strongest applications will have access to a broad range of diseases, patient groups, expertise, and geographic regions not only relating to the pragmatic trial proposed in their application, but also those that would give the greatest likelihood of participating in PCTs proposed by other groups for network-wide implementation. While this may be challenging as the PCTs proposed by other groups will be unknown at the time of application, demonstrating the ability to participate in a wide a range of PCTs will significantly strengthen an application.

Will cancer-related applications be considered for funding?

Given the extensive ongoing work in implementing genomics in cancer treatment, cancer-only trials will be considered non-responsive to the IGNITE II RFAs and will be returned to the applicant. Trials evaluating germline cancer susceptibility as one component in a broader analysis of susceptibility to a variety of diseases may be acceptable. However, applications in which cancer susceptibility is a major component of the proposed analysis will be considered a low priority for NHGRI funding. Applicants are encouraged to contact NHGRI to discuss their proposed trial and patient population before formally submitting their applications.

Are costs for genomic testing allowable?

Yes, genomic testing in a CLIA-compliant manner can be included in the proposed budget. Applicants should be aware of the instructions in Section IV., Application and Submission Information, "R&R or Modular Budget" and "R&R Subaward Budget" that provide guidance on information to be included in the application budget.

What is the scope of responsibility of the coordinating center?

Given that IGNITE II will rely on network adoption of multiple pragmatic clinical trials, the coordinating center will be integral to IGNITE II's successful evaluation of genomic medicine interventions. In brief, the coordinating center will lead, in collaboration with the Clinical Groups, all aspects of network-wide protocol adaptation, execution, and analyses, development and statistical modeling, and final analysis of primary and secondary network-wide clinical trial outcomes in collaboration with the Clinical Groups network-wide. For a full description of the IGNITE II Coordinating Center responsibilities, please refer to the Research Approach and Research Strategy sections of RFA-HG-17-010.

What specific information should the letters of support for each clinical site include?

Letters of support from the Clinical Sites should document commitment from site leadership to participate fully in IGNITE II and are encouraged to demonstrate appropriate commitment and resources such as protected time, facilities, space, or resources for the Clinical Site; describe their experience in enrolling patients in clinical research studies; and provide a summary of the site's research experience and capabilities similar to the format below.

Site Information
Site Name: Site Street Address, City, State:
Project Contact Information
Project Site PI:
Site Characteristics
Please choose the best description of your site (check one): ___Academic Teaching Hospital ___Community Hospital ___Private Practice

___Family Health Clinic ____ Federally-Qualified Community Health Center ____Military

____Other (specify_____)

Which EHR system does your site currently use? ___ Epic ___ Cerner ___Other (specify_____)

What is the usual time (average and range) between request and implementation of electronic clinical decision support for research studies at your site? ____months ____ weeks

Please provide an estimate of the percentage of each age range in the population seen by your clinic:

___infant (<1 yr) ___pediatric (1-17 yrs) ___adult (18 yrs and older)

Are males and females equally represented among your patient population? _____

If no, please briefly describe the gender breakdown among your patient population: _____

Please provide a racial/ethnic breakdown of the population seen by your clinic (i.e. Number (%) Hispanic or Latino, American Indian or Alaska Native, Asian, Black or African American, , Native Hawaiian or Other Pacific Islander, and White):

Does your site have an IRB? ____ Yes ____ No

What is the usual time (average and range) between IRB submission and approval for clinical studies at your site? ____months ____ weeks

Can your site use a central IRB for multi-center clinical trials? ____ Yes ____ No

How many clinical research studies are currently active at your site? _____

How many patients have been enrolled in clinical trials in your site in the past 2 years? ____

How many patients have been enrolled in genetic or genomic research studies in your site in the past 2 years? _____

Please briefly describe any differences in age, gender, or ethnicity between the population seen by your clinic and the population from your clinic enrolled in research studies:

Site Facilities/Equipment:

Does your site have access to a CLIA certified clinical lab for genetic testing? ____ Yes ____ No

If yes, name and address of CLIA lab proposed for this study: _____

If yes, please briefly describe the genetic testing capabilities of your site's CLIA lab (i.e. microarray, NGS, etc.):

Does your site perform genetic testing through a third party clinical lab(s)?

If yes, please briefly describe the types of genetic testing sent to third party clinical labs and list which lab(s) your site uses:

(Optional) Please provide any additional information relevant to your site's ability to participate in genomic medicine pragmatic clinical trials:

How should the clinical settings and characteristics of clinical sites within an applicant's Clinical Group be described?

Applicants should provide a summary table describing the Clinical Sites comprising their Clinical Group that lists the clinical setting (e.g. academic institution, community hospital, primary care practice, etc.) and the site's characteristics. A table similar to the sample below may be useful for organizing and providing this information.

		Total N (%)	Site 1	Site 2	Site 3	Site 4
EHR Type	Epic					
	Cerner					
	Other (describe)					
Site types (Please select one)	Academic institution					
	Community Hospital					
	Primary Practice					
	Family Health Clinic					
	Federally-Qualified Community Health Center					
	Military					
	Other (Specify)					
Site demographics	Sample size for proposed PCT					
	Sample size for other network-wide PCTs					

Ethnicity of patient population	Hispanic or Latino					
Race of patient population	Black or African American					
	American Indian/ Alaska native					
	Asian					
	Native Hawaiian/ Pacific Islander					
	White					
	Population < 18 yrs					
	Median and age range of adult population (18 and above)					

Why is the ethical, legal and social implications (ELSI) research component being funded separately through a supplement?

To ensure that the network-wide ELSI research study is relevant to the pragmatic clinical trials selected for implementation, the ELSI research study will be developed after the PCTs are prioritized and selected to go forward. The ELSI research study will be collaboratively developed by the CGs after award based on the most significant ELSI issues in the selected PCTs and the strengths of the IGNITE II Network. The ELSI research study should not be proposed in the current application. However, applicants should describe unique strengths of the proposed research team, including experience conducting ELSI research.

How will the pragmatic clinical trials to be implemented network-wide be selected?

Network-wide pragmatic clinical trial protocols proposed by applicants will be prioritized after award by a Protocol Review Committee (PRC), which will include experts in genomic medicine, clinical trial design, biostatistics, outcome measures, and other areas of expertise as needed, and relevant stakeholders. The PRC will provide a written critique of each proposal and a final prioritization to the NHGRI. Once protocols are selected to move forward, the Steering Committee, comprising the Principal Investigators of each group, the CC PI, and NHGRI personnel, will then adapt prioritized protocols for expansion across the IGNITE II Network.

Does my pragmatic clinical trial need to involve randomization (of patients and/or clinical sites)?

Randomization of patients and/or clinical sites to a control or intervention arm(s) is expected. Investigators considering proposing a non-randomized trial must provide a strong justification during their pre-application discussions with NHGRI staff.