Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
National Institutes of Health (NIH)
U.S. Department of Health and Human Services (HHS)

Frequently Asked Questions for the NICHD Genomic Clinical Variant Expert Curation Panels Request for Applications (RFA)

What is the objective of the RFA?

The objective of the RFA-HD-17-001 Funding Opportunity Announcement (FOA) is to:

- Establish expert curation panels that will select candidate genes and genomic variants associated with diseases or conditions of high priority to NICHD that will have a high impact on clinical practice in these areas
- Analyze all relevant data utilizing the ClinGen (https://www.clinicalgenome.org) resource tools and based on this analysis
- Establish the clinical actionability of individual genes and/or variants to support clinical practice

What are the priority conditions or diseases for NICHD curation panels?

For the purpose of this FOA, genes and variants should be associated with but not limited to one or more of the following topic areas: reproductive and gynecological health; poor pregnancy outcomes; high risk newborn conditions; structural birth defects; intellectual and developmental disabilities; and susceptibility to infection. Genes for conditions that are more appropriate to other Institutes or Centers such as childhood cancer, cardiac anomalies, or hearing loss are not responsive to this RFA. A more detailed list of NICHD high priority areas are identified by the Extramural Scientific Branches. This list can be found at https://www.nichd.nih.gov/about/org/der/branches/Pages/index.aspx. Please contact Danuta Krotoski at krotoskd@mail.nih.gov or 301 496-55765 if you have any questions about responsiveness to this RFA.

How should the expert panel select the genes or variants to be curated?

Selection of genes or variants is at the discretion of the chair and panel members. It is anticipated that the expert panel will identify the genes/variants within the selected domain. There is no set number of genes. With only three years of funding, consideration should be taken of the scope of clinical domain/disorder and the number of genes or variants to be curated. The panel should identify those genes that are most likely to impact clinical practice and for which evidence is available. The justification for selecting the genes and or variants that have been identified should be based on this principle rather than a sample of convenience.

What is the leadership structure and are Multiple Principal Investigators (PIs) allowed?

It is anticipated that the PI will also serve as chair of the expert panel and in some cases, may have a co-chair to help lead the panel's activities. Though it does not explicitly exclude multiple PIs, the RFA states that funds are available to support partial salary of the PI who serves as the expert panel chair of the working group and under exceptional circumstances, a co-chair.

Who should participate on the expert panel?

For the purpose of this FOA, membership of the expert panel should include domain and condition experts who reflect the breath of expertise required to ascertain the clinical actionability of the genes identified. The panels should include medical professionals, medical geneticists, clinical laboratory diagnosticians and/or molecular pathologists, researchers and statisticians. Since the goal of the RFA is to assess the clinical validity of the selected gene-disease associations or genetic variant pathogenicity based on current knowledge that could support guidelines for clinical practice, multiple institutions and organizations must be represented and international participation is strongly encouraged. Additional members of the expert panel curation team should include a project coordinator, biocurators and bioinformatics specialist(s) who will provide materials to the curation panel.

Can all members of the expert panel be from the same institution?

No. To qualify for an NICHD expert panel, members are expected to be from multiple institutions, and foreign members are encouraged. In this regard, NICHD is following the ClinVar Expert Panel guidance: https://www.clinicalgenome.org/expert-groups/.

What if other groups/panels are evaluating the same domain or group of genes?

PIs are encouraged to work with the other groups to establish a single working group rather than duplicating effort. If this cannot be accomplished, a justification must be provided as to why the work of this panel will be unique, and any area of overlap must be described. As the goal of the RFA is to provide expert panel evaluation of gene-disease or variant pathogenicity assessments to support variant curation, having two groups duplicate efforts is not an efficient use of resources.

How should conflicts of interest be managed?

Conflicts of interest should be identified for each member of the working group and managed by the Curation Panel PI and the PI's institution.

How should expert panels be structured?

The investigators are expected to identify genes or variants within a clinical domain of priority to NICHD (https://www.nichd.nih.gov/grants-funding/opportunities-mechanisms/areas-research/Pages/default.aspx). Depending on the number of genes or variants, either a single panel could meet regularly to review individual genes/variants or establish subpanels that will focus on specific subsets of genes/variants. These subpanels/working groups could then report to the entire expert panel to determine final assertions. The investigators should build on the experience of ClinGen Clinical Domain Working Groups (CDWG) and curation panels in organizing the work of the expert panel. An example of how ClinGen structures curation working groups can be found at https://clinicalgenome.org/about/clingen-curation-activities-overview/ and in the webinar presentation slides (https://www.nichd.nih.gov/grants-funding/opportunities-mechanisms/active-foa/tech_assist/Pages/default.aspx).

How should expert panel members be listed in the application?

Each member of the expert panel should be listed under personnel as consultants with a biosketch attached. Consultants do not require an E-commons name and are paid nominal fees.

Who should staff the expert panels?

The PI (and possibly co-PI) will be responsible for leading the panels. However, experience has shown that the availability of a project coordinator, biocurator, and bioinformatician greatly enhances the efficiency of the curation panel. The biocuration staff is expected to perform data collection and primary analyses for projects. These may be genetic counselors, clinical fellows or researchers in the field. In addition, bioinformatics specialists should be engaged. Both the biocurators and bioinformatics specialists are expected to utilize the ClinGen tools and to participate on appropriate ClinGen working groups.

What are the allowable costs?

Partial salary support for expert panel chair and under exceptional circumstances, the co-chair, is allowed. Both domestic and international panel members can receive nominal consulting fees. The primary emphasis should be on supporting a project coordinator, biocurators and bioinformatics specialists. Funds can be used for meeting support or to travel to face-to-face meetings of the expert panel, which can take place at regularly attended conference by panel members. In addition the by the PI and other appropriate members should plan on attending the annual ClinGen/Decipher meeting. There may be additional costs associated with training on ClinGen tools. Regarding budgeting for consultants, if they will not be conducting a substantive portion of the research, their fees will not be considered as a sub-award, and therefore, no indirect costs would be involved. If they are conducting a substantive portion of the research, a subcontract will be required. All costs, including indirect costs, come from the parent award.

How will NICHD expert curation panels interface with ClinGen and ClinVar?

Expert curation panels are expected to utilize the ClinGen framework and curation tools to assess current evidence supporting disease association for the chosen genes and variants. Expert panel curation staff are expected to receive training on ClinGen tools and resources through distance and in-person educational modules (under development). The PI and curation staff are expected to participate on appropriate ClinGen working groups and to deposit final determinations and supporting evidence into ClinGen and ClinVar databases. Applicants are encouraged to review the Pre-Application Webinar slides for further information about ClinGen tools and to visit the ClinGen sites: https://clinicalgenome.org/about/clingen-curation-activities-overview/; https://clinicalgenome.org/events-news/clingen-in-the-news/announcing-nichd-funding-opportunity-and-demo-clingen-curation-tools/ and the ClinGen helpdesk: clingen-helpdesk@lists.stanford.edu.

How will NICHD expert curation panels be integrated into ClinGen

ClinGen's Clinical Domain Working Groups (CDWG) serve a strategic and organizational function for horizon scanning and fostering the expert curation groups. Each CDWG includes one or more expert panel groups undertaking gene or variant curation, and is an umbrella over a cluster of related expert panels. ClinGen has proposed the following options for integration of NICHD expert curation panels with ClinGen activities based on NICHD/National Human Genome Research Institute and ClinGen review: placement within an existing ClinGen CDWG if appropriate; formation of a new CDWG if appropriate; or support of a standalone "expert panel."

What ClinGen and ClinVar resources are available to guide and facilitate the curation process?

ClinGen has posted guidelines for expert panel status in ClinVar that describes the process of curation and criteria for the levels of submission of clinical assertions as well as an expert panel toolkit: https://www.clinicalgenome.org/expert-groups/. In addition, ClinGen has provided Demonstration Curation interfaces https://www.clinicalgenome.org/events-news/clingen-in-the-news/announcing-nichd-funding-opportunity-and-demo-clingen-curation-tools/. For further information about these interfaces please contact the ClinGen help desk at: clingen-helpdesk@lists.stanford.edu.

How best to contact ClinGen?

The ClinGen helpdesk can provide guidance on ClinGen tools and resources: clingen-helpdesk@lists.stanford.edu.

NICHD Contacts:

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