

Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)
National Institutes of Health ([NIH \(http://www.nih.gov\)](http://www.nih.gov))

Components of Participating Organizations
National Human Genome Research Institute ([NHGRI \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82470\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82470))

Note: Not all NIH Institutes, Centers, and Offices (ICOs) participate in Announcements. Applicants should carefully note which ICOs participate in this announcement and view their respective areas of research interest at the [ICO-Specific Scientific Interests website \(https://grants.nih.gov/funding/find-a-fit-for-your-research/nih-institutes-centers-offices\)](https://grants.nih.gov/funding/find-a-fit-for-your-research/nih-institutes-centers-offices). ICOs that do not participate in this announcement will not consider applications for funding.

Funding Opportunity Title
Genomic Variant Interactions With Other Variants Or The Environment (UM1 Clinical Trials Not Allowed)

Activity Code
[UM1 \(http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search_Type=Activity&Search.x=0&Search.y=0\)](http://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search_Type=Activity&Search.x=0&Search.y=0) Research Project with Complex Structure Cooperative Agreement

Announcement Type
New

Related Notices

- Check for any recent [Notices of NIH Policy Changes \(https://grants.nih.gov/grants/guide/url_redirect.php?id=11163\)](https://grants.nih.gov/grants/guide/url_redirect.php?id=11163) that may impact application requirements.

Funding Opportunity Number (FON)
RFA-HG-27-009

Companion Funding Opportunity
[RFA-HG-27-007 \(https://www.grants.gov/search-results-detail/358854\)](https://www.grants.gov/search-results-detail/358854), [UM1 \(https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search.x=0&Search.y=0&Search_Type=Activity\)](https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search.x=0&Search.y=0&Search_Type=Activity) Research Project with Complex Structure Cooperative Agreement
[RFA-HG-27-008 \(https://www.grants.gov/search-results-detail/358855\)](https://www.grants.gov/search-results-detail/358855), [U24 \(https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U24&Search.x=0&Search.y=0&Search_Type=Activity\)](https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=U24&Search.x=0&Search.y=0&Search_Type=Activity) Resource-Related Research Project (Cooperative Agreements)
[RFA-HG-27-010 \(https://www.grants.gov/search-results-detail/359170\)](https://www.grants.gov/search-results-detail/359170), [UM1 \(https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search.x=0&Search.y=0&Search_Type=Activity\)](https://grants.nih.gov/grants/funding/ac_search_results.htm?text_curr=UM1&Search.x=0&Search.y=0&Search_Type=Activity) Research Project with Complex Structure Cooperative Agreement

Number of Applications
See Part 2, Section III. 3. Additional Information on Eligibility.

Assistance Listing Number(s)
93.172

Funding Opportunity Purpose
The purpose of this Notice of Funding Opportunity (NOFO) is to solicit applications to study the effects of genetic or environmental interactions on genomic variant impact. To accomplish this, interaction centers will first propose a research framework to investigate whether interactions with effects beyond additive are important modifiers of the impact of variants. Centers will apply their framework to experimentally test combinations for interactions and share their data as well as analyses through the Impact of Genomic Variation on Function (IGVF) portal and catalog. Centers will share their method for predicting the most important combinations for future testing. The rationale for this combination of research and resource work is the identification of a structure within the interaction landscape might result in better predictions of the most important interactions to test, leading to more effective variant testing, better understanding of genome-wide association studies (GWAS), and improved polygenic scores. As IGVF Consortium members, centers will work together to ensure all consortium resources are accessible to a wide variety of potential users. Centers are also expected to collaborate with other consortium components to coordinate assays, variants, and cell types, and to develop shared analysis strategies to meet consortium goals.

Funding Opportunity Goal(s)
As a leading authority in the field of genomics, the mission of the National Human Genome Research Institute (NHGRI) is to accelerate scientific and medical breakthroughs that improve human health by driving cutting-edge research, developing new technologies, and studying the impact of genomics on society. Congress initially established NHGRI to characterize the structure and function of the human genome, including the mapping and sequencing of individual genes. This also includes reviewing and funding research proposals, developing training programs, coordinating international genome research, communicating advances in genome science to the public, and reviewing and funding proposals to address the ethical and legal issues associated with this research. NHGRI supports the development of methods, resources and technologies to improve the health of all humans through advances in genomics research. NHGRI supports research that accelerates foundational resources, technology development, and experimental and computational approaches for basic genomics and functional genomics research; for the application of genomics to medical science and clinical care; and to support ethical, legal and social implications (ELSI)

Key Dates

Posted Date					
October 09, 2026					
Open Date (Earliest Submission Date)					
November 14, 2026					
Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS - New/Renewal/Resubmission/Revision, as allowed	Scientific Merit Review	Advisory Council Review	Earliest Start Date
December 14, 2026	Not Applicable	Not Applicable	July 2027	August 2027	September 2027

All applications are due by 5:00 PM local time of applicant organization.

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

No late applications will be accepted for this Notice of Funding Opportunity (NOFO).

Expiration Date					
December 15, 2026					
Due Dates for E.O. 12372					
Not Applicable					

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), except where instructed to do otherwise (in this NOFO or in a Notice from [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164)).

Conformance to all requirements (both in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) and the NOFO) is required and strictly enforced. Applicants must read and follow all application instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the [NIH ASSIST system \(https://public.era.nih.gov/assist/public/login.era\)](https://public.era.nih.gov/assist/public/login.era) to prepare, submit and track your application online.
2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and [eRA Commons \(https://public.era.nih.gov/commons/\)](https://public.era.nih.gov/commons/) to track your application. Check with your institutional officials regarding availability.
3. Use [Grants.gov \(https://www.grants.gov/search-results-detail/358854\)](https://www.grants.gov/search-results-detail/358854) Workspace to prepare and submit your application and [eRA Commons \(http://public.era.nih.gov/commons/\)](http://public.era.nih.gov/commons/) to track your application.

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Part 2. Full Text of Announcement

Section I. Notice of Funding Opportunity Description

Background

A major challenge in genomics is defining the role of genomic variation in influencing phenotypes in human biology and diseases. As outlined in [NHGRI's 2020 Strategic Vision \(https://www.genome.gov/2020SV\)](https://www.genome.gov/2020SV), studies characterizing the functional consequences of variants have not kept pace with studies of variant discovery or association, and this lack of functional genomic information remains a barrier that impedes progress in genomics.

The Impact of Genomic Variation on Function Consortium (IGVF) was established in 2021 to address the challenge of understanding how genomic variation affects genome function to influence phenotypes using a coordinated team-science approach. The program utilizes emerging experimental and computational genomic approaches to build a catalog of the impact of genomic variants on genome function and phenotypes and to share data and other resources with the scientific community.

Program Goals and Notices of Funding Opportunity (NOFOs)

NHGRI is issuing an open call for applications to participate in a second phase of IGVF, based on recent [community recommendations on functional variant interpretation](#) and input from the [National Advisory Council for Human Genome Research](#). The goals of the second phase of IGVF are to:

- Test the impact of individual genomic variants on function
- Study the effects of genomic variation interactions on function
- Model and predict the impacts of genomic variation on function and phenotype
- Expand a set of resources to enable future studies

To achieve these goals the following NOFOs are issued:

- Systematic Characterization of Genomic Variation to Assess Effects of Individual Variants on Genome Function and Phenotype – [RFA-HG-27-007 \(https://www.grants.gov/search-results-detail/358854\)](#)
- Genomic Variant Interactions With Other Variants Or The Environment – [RFA-HG-27-0090 \(https://www.grants.gov/search-results-detail/359277\)](#)
- Computational Modeling and Analysis of the Impact of Genomic Variation on Function – [RFA-HG-27-010 \(https://www.grants.gov/search-results-detail/359170\)](#)
- IGVF Data and Coordinating Center – [RFA-HG-27-008 \(https://www.grants.gov/search-results-detail/358855\)](#)

NHGRI encourages all investigators with ideas aligned with the goals of this NOFO to submit applications.

Research Scope and Objectives

Current understanding of the interactions of genetic variants with other variants, or with the environment, is limited. In molecular studies (e.g. genetics using model organisms, functional genomics, and protein engineering) interactions beyond additive effects such as epistasis or synergy are sometimes detected. However, investigation of human diseases and traits using statistical methods such as GWAS find a minimal contribution from effects beyond additive. At least superficially, there is tension between these sets of findings. Do interactions beyond additive contribute to human traits and human disease, and if so, how prevalent is that contribution, and what are specific examples of such interactions? Using perturbations to test all by all (or higher orders of variant interaction) is not possible with current technologies. However, if interactions beyond additive are important for human traits and diseases, and if there is structure within the interaction landscape where non-additive interactions are enriched, these centers might identify the subspace of interactions that are most informative to test using perturbations, leading to more effective variant testing, better understanding of GWAS, and improved polygenic scores.

The objectives for this NOFO are to:

- Propose a theoretical and quantitative framework for assessing interactions.
- Apply the proposed framework to characterize interactions.
- Contribute results of tested variant combinations as well as models for predicting the most important combinations to test as part of the IGVF catalog.

The scope of this NOFO also includes the following:

- Enable others to perform related studies using these approaches
- Improve generalizable approaches or technologies for high-throughput assays (optional)

A theoretical and quantitative framework for assessing interactions: Interaction centers should be grounded in a framework to test phenotypic joint variant effects or joint effects of variants with environments. Frameworks should be theoretically grounded (e.g. quantitative or evolutionary genetics) categorize interactions (examples include additive, superadditive, epistatic/hypostatic), and be compatible with high-throughput variant testing.

Characterizing Interactions: Interaction centers should implement at least one system high-throughput testing of interactions. There should be a systematic and efficient strategy for subsampling the space of all possible combinations taking into account evidence from human genetics and biological function. Examples of joint variant tests include combinations of variants within and between loci (e.g., cis and trans effects), combinations of variant types (e.g., coding and non-coding variants, rare and common alleles), testing variants across genetic backgrounds (e.g., testing variants across a range of local or global genetic ancestry). Examples of joint variant and exposure tests include the impact of inflammation, stress, or altered metabolism on variant penetrance. (Note, for this RFA, testing a set of variants across cell types is not responsive.) Combinations could be pairwise or higher order. Interactions may be tested at the level of genes, regulatory elements, or variants. Interaction centers may propose to detect phenotypic changes at one or more scales, such as molecular (e.g., RNA abundance or kinase activity), cellular (e.g., morphology), multi-cellular (phenotypes that require interaction of more than one cell type, which need not be cell autonomous phenotypes), or organismal phenotypes (e.g., behavior or development). Interaction centers may test one or more classes of variants (examples include common, rare, disease associated, synthetic), using at least one high-throughput assay for testing (examples include reporters, epigenome editing, genome editing), and at least one phenotype for detecting responses (examples include RNA-seq, survival, a cellular response). Interaction center assays and data processing pipelines should be in production by the end of the first year of funding.

Contribute results of tested variant combinations as well as models for predicting the most important combinations to test as part of the IGVF catalog: The primary goal of the consortium is to collaboratively produce a variant/element/phenotype catalog for use by the community. Interaction centers will contribute data and results for variants and interactions that were tested. Interaction centers will submit raw data, processed data, metadata, and integrative analysis to the resource. This catalog will report the perturbation and phenotype assay(s), the biological system(s), results and interpretation. Recipients will collaborate with the IGVF Data and Coordinating Center (DACC) about representations of their data and analyses and specify use cases that should be supported by the catalog.

Enable others to perform related studies using these approaches: Interaction centers will fully share data and analyses; in addition, they will share with the community the algorithms, software, protocols, models and technologies used to create the data and analyses. The consortium will assess the experimental and computational approaches used. This may include the specificity, sensitivity, accuracy and generalizability of approaches. It may also include determining the systematic limitations and biases as well as strengths of the approaches. The consortium may identify what is needed to improve future assessments of the role of genetic variation in genome function. This could be a joint effort across interaction centers, if scientifically appropriate.

Improve generalizable approaches or technologies for high-throughput assays (optional): This NOFO is NOT a technology development opportunity; Interaction centers must perform their their major data collection based on methods that are ready at the time of funding. However, Interaction centers may use a small portion of their resources (not to exceed 5%) to develop or refine experimental and computational approaches. Refinement of existing assays or development of new orthogonal assays for validation are examples. Technology development under this NOFO is limited to approaches for characterization of functional genomic elements that are high-throughput, generalizable across experimental systems and disease, with the potential to implement during the current project period.

Consortium Formation and Coordination

This NOFO uses the [cooperative agreement award instrument \(https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.3.3_types_of_award_instruments.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.3.3_types_of_award_instruments.htm). Interaction centers will become members of the IGVF Consortium. Consortium members are expected to work collaboratively with NHGRI and all members of the consortium towards meeting consortium goals, in addition to the specific research goals outlined in their individual applications.

Members of the IGVF Consortium will work together to:

- Develop of a catalog of the impact of genomic variants on genome function and phenotypes.
- Plan experiments, implementing studies, and analyze results from within component and consortium-wide projects, typically through working groups.
- Develop agreed-upon standards and metrics for data, metadata, data quality, and analyses.
- Contribute all data, metadata, protocols, methodologies, analyses, software, and other products to the IGVF Data and Coordinating Center (DACC) in specified formats.
- Share best practices and lessons learned within the consortium and with the external community.
- Lead and actively participating in consortium-wide, Steering Committee, and working group meetings.
- Contribute to training across the consortium, cross-consortia efforts, and broader outreach efforts.

Consortium members are expected to coordinate assays, variants, and cell types and to develop shared analysis strategies and uniform computational workflows, when applicable, to meet consortium goals, rather than function as independent projects with independent goals. When appropriate, selection of variants and cell types in this second program phase should be done in consideration of variants and cell types characterized in the first phase of IGVF (see: <https://data.igvf.org/resources/>). IGVF research is limited to mammalian systems, with a preference for human studies including samples derived from individuals across a breadth of genetic ancestries and the consideration of sex as a biological variable. Variants selected for testing should account for allele frequencies and disease associations within and across human populations. Proposed cell types and states should be derived from tissues important in development, differentiation, or human diseases.

A central goal of IGVF is the development of data, tools, and other resources that can be used by researchers not funded by this program. Consortium members will be expected to generate pipelines, tools, and educational materials that facilitate community uptake of IGVF data and methods, and to work together to ensure all consortium resources are accessible to a wide variety of potential users. Data, predictions, and models should be shared early and organized in ways that enable a variety of uses by the broader scientific community, from searches of individual variant impacts to large scale integrative or machine learning approaches.

Consortium members will also be expected to continue to collaborate with other projects and consortia with interests in variant interpretation and coordination across resources, especially in efforts to develop shared data processing and analysis pipelines to enable data sharing and comparisons. This includes work with the Atlas of Variant Effects ([AVE](#)) Alliance, The Molecular Phenotypes of Null Alleles in Cells (MorPhiC), the Clinical Genome ([ClinGen](#)) Resource, the Genomics Research to Elucidate the Genetics of Rare Diseases ([GREGoR](#)), the Human Pangenome Reference Consortium ([HPRC](#)), and other consortia, as relevant.

Consents and Data Sharing in IGVF

A key deliverable of IGVF is the development of two public data resources, the IGVF Catalog and Data Portal. To facilitate user access to these resources, NHGRI expects that centers will prioritize the use of samples derived from research participants that have been consented for the broadest possible sharing of genomic data, such as consent for unrestricted access, or for general research use and broad sharing through controlled access. Consent language should also avoid restrictions on the types of users who may access these data for genomics research.

To Learn More

A webinar will be held where NIH staff will present overviews of IGVF NOFOs and answer NOFO-related questions from prospective applicants. Time, date, and webinar links will be made available through a Notice in the NIH Guide. The webinar is open to all prospective applicants, but participation is not required to apply.

Prospective applicants are strongly encouraged to contact the email address listed as the Scientific/Research Contact(s) below to discuss the responsiveness and alignment of their proposed work with program goals.

Applications Not Responsive to this NOFO

The following types of applications are not responsive to this NOFO and will not be reviewed:

- Applications that propose to test a set of variants across cell types as an approach to study interactions.
- Applications that are primarily developing new experimental methods, or that are dependent upon the development of new experimental methods
- Applications that do not use biological systems relevant to human health and disease.
- Applications that focus on mechanistic studies or particular genes, biological systems or diseases.
- Applications that do not indicate plans to collaborate with and contribute to consortium-wide, collaborative activities and analyses throughout the course of the project.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Cooperative Agreement: A financial assistance mechanism used when there will be substantial Federal scientific or programmatic involvement. Substantial involvement means that, after award, NIH scientific or program staff will assist, guide, coordinate, or participate in project activities. See Section VI.2 for additional information about the substantial involvement for this NOFO.

Application Types Allowed

New

The [OER Glossary \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11116\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11116) and the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) provide details on these application types. Only those application types listed here are allowed for this NOFO.

Clinical Trial?

Not Allowed: Only accepting applications that do not propose clinical trials. Note: Applications may propose activities involving human subjects that are not deemed clinical trials.

[Need help determining whether you are doing a clinical trial? \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82370)

Funds Available and Anticipated Number of Awards

NHGRI intends to commit \$10M total costs in FY 2027 to fund 5 awards.

Award Budget

Application budgets must not exceed \$1.5M direct costs per year. Application costs must reflect the actual needs of the proposed project.

Award Project Period

The maximum project period is five years.

NIH grants policies as described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120) will apply to the applications submitted and awards made from this NOFO.

Section III. Eligibility Information

1. Eligible Applicants

Eligible Organizations

Higher Education Institutions - Includes all types

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Local Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)

Federal Governments

- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Organizations)

Foreign Organizations/Foreign Collaborations

Non-domestic (non-U.S.) Entities (Foreign Organizations) **are** eligible to apply.

Non-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

Foreign components, as [defined in the NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11118), **are** allowed.

NIH will no longer issue awards (i.e., new, renewal, or non-competing continuation) to domestic or foreign entities that involve foreign subawards/subcontracts. All NIH-funded research involving foreign subawards/subcontracts must be submitted in response to a NOFO that is specifically designated for funded international collaborations. See [NIH Grants Policy Statement 16.8 Collaborative International Research Awards \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_16/16.8_collab_int_res_awards.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_16/16.8_collab_int_res_awards.htm).

Applications involving foreign subawards/subcontracts submitted in response to this NOFO will be deemed noncompliant and will not be considered for funding. This policy applies to all monetary international collaborations resulting in foreign subawards/subcontracts, however, it does not preclude unfunded international collaborations or [foreign components \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_1/1.2_definition_of_terms.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_1/1.2_definition_of_terms.htm), funding for foreign consultants, or procurement of unique equipment or supplies from foreign vendors.

Required Registrations

Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. Failure to complete registrations in advance of a due date is not a valid reason for a late submission, please reference [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423) for additional information

- [System for Award Management \(SAM\) \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82390\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82390) – Applicants must complete and maintain an active registration, **which requires renewal at least annually**. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and

Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code. Foreign organizations must obtain a [NATO Commercial and Government Entity \(NCAGE\) Code](#) (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11176) (in lieu of a CAGE code) in order to register in SAM.

- Unique Entity Identifier (UEI)- A UEI is issued as part of the SAM.gov registration process. The same UEI must be used for all registrations, as well as on the grant application.
- [eRA Commons](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=11123) - Once the unique organization identifier is established, organizations can register with eRA Commons in tandem with completing their Grants.gov registrations; all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.
- [Grants.gov](#) (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82300) – Applicants must have an active SAM registration in order to complete the Grants.gov registration.

Program Directors/Principal Investigators (PD(s)/PI(s))

All PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or to affiliate their existing account with the applicant organization in eRA Commons. Obtaining an eRA Commons account can take up to 2 weeks.

All PD(s)/PI(s) must be registered with [ORCID](#) (<https://orcid.org/>). The personal profile associated with the PD(s)/PI(s) eRA Commons account must be linked to a valid ORCID ID. For more information on linking an ORCID ID to an eRA Commons personal profile see the [ORCID topic in our eRA Commons online help](#) (<https://era.nih.gov/erahelp/Commons/default.htm#orcid.htm%3FTocPath%3D29>).

Eligible Individuals (Program Director/Principal Investigator)

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with their organization to develop an application for support.

For institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and submission details in the Senior/Key Person Profile (Expanded) Component of the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

2. Cost Sharing

This NOFO does not require cost sharing as defined in the [NIH Grants Policy Statement NIH Grants Policy Statement Section 1.2 Definition of Terms](#). (http://grants.nih.gov/grants/guide/url_redirect.htm?id=11126).

3. Additional Information on Eligibility

Number of Applications

Applicant organizations may submit more than one application, provided that each application is scientifically distinct.

The NIH will not accept duplicate or highly overlapping applications under review at the same time, per [NIH Grants Policy Statement Section 2.3.7.4 Submission of Resubmission Application](#) (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82415). This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see [NIH Grants Policy Statement 2.3.9.4 Similar, Essentially Identical, or Identical Applications](#) (http://grants.nih.gov/grants/guide/url_redirect.htm?id=82423)).

Section IV. Application and Submission Information

1. Requesting an Application Package

The application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional system-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this NOFO. See your administrative office for instructions if you plan to use an institutional system-to-system solution.

2. Content and Form of Application Submission

It is critical that applicants follow the instructions in the Research (R) Instructions in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) except where instructed in this notice of funding opportunity to do otherwise (in this NOFO, in a [policy notice](#) (https://grants.nih.gov/grants/guide/url_redirect.php?id=11163), or other notice from [NIH Guide for Grants and Contracts](#) (https://grants.nih.gov/grants/guide/url_redirect.php?id=11164)). Conformance to the requirements in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for review.

Page Limitations

All page limitations described in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) and the [Table of Page Limits](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=61134) must be followed.

For this specific NOFO, the Research Strategy is limited to 30 pages (exclusive of the Specific Aims page).

Instructions for Application Submission

The following section supplements the instructions found in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) and should be used for preparing an application to this NOFO.

SF424(R&R) Cover

All instructions in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Project/Performance Site Locations

All instructions in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Other Project Information

All instructions in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

SF424(R&R) Senior/Key Person Profile

All instructions in the [How to Apply - Application Guide](#) (https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

The PD(s)/PI(s) must designate a dedicated Project Manager to direct the day-to-day operations of the Coordinating Center. A PD/PI may serve as the Project Manager.

R&R Budget

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

- For single PD/PI applications, the PD/PI is expected to devote at least 3 person months, based on a 12-month calendar. If multi-PDs/PIs are proposed, then each PD/PI is expected to commit sufficient time to serve his/her proposed role, with a minimum aggregate PD/PI effort of 3 person months, and at least one PI devoting 2 months. The appropriateness of the effort of key personnel must be justified in the budget justification.
- Budgets should include support for a dedicated Project Manager who will devote a minimum of 4 person months, based on a 12-month calendar, to oversee the day-to-day activities of the center, coordinate metadata and data submissions to the DACC, coordinate center participation in integrative analysis, coordinate across center sites, if applicable, and be responsible for promptly providing requested reporting information to NHGRI Program Staff. A PD/PI may serve as the Project Manager.
- Budgets should include funds for the PD(s)/PI(s) and key personnel to attend the initial consortium kickoff meeting, as well as for the PD(s)/PI(s) and 2-6 members of the center to attend annual consortium meetings.
- Budgets should include any funds required to support sharing of scientific data under this NOFO. This should include funds to prepare data for submission to the IGVF DACC and the IGVF data portal. NIH provides guidance on allowable costs for data management and sharing [here \(https://sharing.nih.gov/data-management-and-sharing-policy/planning-and-budgeting-for-data-management-and-sharing/budgeting-for-data-management-sharing\)](https://sharing.nih.gov/data-management-and-sharing-policy/planning-and-budgeting-for-data-management-and-sharing/budgeting-for-data-management-sharing). For projects generating genomic data derived from research participants, investigators should consider costs associated with complying with the NIH and NHGRI GDS Policy expectations (e.g., obtaining samples with explicit informed consent for future research use and broad data sharing, implementing processes to seek new consent from study participants, etc.).
- Applicants must set aside 20% of the direct costs for each year of the award to support collaborative work in consultation with and with approval by NHGRI staff. This work is anticipated to further the needs of the IGVF Consortium and the genomics research community.

R&R Subaward Budget

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

PHS 398 Cover Page Supplement

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

PHS 398 Research Plan

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed, with the following additional instructions:

Specific Aims:

Describe the specific goals of the Interaction Center and its role in achieving the overall objectives of the IGVF Consortium.

Research Strategy:

In the Research Strategy, applicants should propose plans, approaches, and potential alternative strategies for carrying out the goals of the Interaction Center. The Research Strategy must be uploaded as a single PDF attachment, and should include the following subsections. (Overview may be included as part of Significance; Management plan may be included as part of Investigator; Framework, Selection, Perturbation methods, Model, Contributing, Enable, and Improvement may be included as part of the approach.)

Overview

Applicants must provide a high-level view of the proposed project including:

- The goals of the proposed project
- Expected outcomes relative to the overall IGVF consortium goal of improving our understanding of the relationships between sequence variation and genome function
- Expected outcomes from this center relative to integration with the IGVF Consortium to achieve the IGVF Consortium goal of improving our understanding of the relationships between sequence variation and genome function to be achieved through integration with IGVF Consortium. Examples could include adopting common assays, developing shared data processing pipelines, collaborating
- Expected outcomes from this center relative to the IGVF Consortium goal of generating a variant/element/phenotype catalog for the community
- Expected outcomes from this center relative to the IGVF Consortium goal of enabling functional genomics studies by researchers outside the IGVF Consortium.

Management plan

- Applicants must describe the organization of the proposed center and its management structure, including integration of tasks to maintain efficient operation and key personnel. This plan should include a description of the overall leadership, decision-making process, as well as the role of the project manager responsible for day-to-day operations. Personnel responsible for key tasks, such as data collection by data type; data analysis by data type; submission of raw data, processed data, metadata, and analyses to the DACC; as well as the project manager should be identified. The reporting relationship for these personnel should be described. Management of consortium activities should be detailed. Management of external collaborations, if any, should be described.
- Applicants should propose quantitative milestones for tracking all aspects of project (including data collection, data submission, integrative analysis, and contribution to overall consortium products starting with the first year of funding), metrics for assessing progress, as well as the expected timeline of progress. Mechanisms for reporting progress to NIH should be described.
- Applicants should propose and describe a LIMS system to track data production, as well as submission of metadata, data (raw and processed) and analyses to the DACC (described in RFA-HG-25-019). A description of the informatics infrastructure for managing data, metadata, analyses, quality control and tracking to support the proposed activities should also be provided.
- Applicants should provide an overview of sharing protocols, software, data and analyses with the community (details are to be described in the Resource Sharing Plan Section and in the Data Management and Sharing Plan (DMS Plan) of the Other Plan(s) Section.
- The management plan should discuss past experiences (if any) in working as part of interdisciplinary teams and/or in large collaborative projects. NIH requires all MPI applications to provide a separate Multiple PD/PI Leadership plan; this may result in some information being reported in more than one location.

Theoretical and quantitative framework for assessing interactions

Applicants must propose a theoretically grounded, quantitative framework for detecting and interpreting the joint effects of variants or joint effects of variants and exposures.

This plan should:

- Describe how to test joint effects
- Define interactions; examples include additive, effects beyond additive, epistasis/hypostasis
- Explain how interactions will be classified using experimental data
- (optional) Describe how the results will be used to predict untested joint effects

Selection of interactions for systematic testing

Applicants must propose a plan to select genomic variants and/or elements for systematic testing of interactions. These projects are intended to be hypotheses generating/discovery science rather than testing specific hypotheses or mechanisms.

This plan should:

- Describe the type of interactions tested by the center (examples include variants interacting with variants, Variants interacting with genetic backgrounds, variants interacting with environment)
- Describe the scale of interaction testing (for example, pairwise combinations or higher order; variants, elements, genes, or a mixture)
- Describe the use of state-of-the-art methods and analyses with the ability to deliver useful data and analyses to the community from the first year of the project. (Projects cannot be dependent on the success of new technologies or approaches.)
- Describe the intellectual framework used to select variants
- Explain the rationale for the selected balance of non-coding or protein-coding variants or elements
- If appropriate, explain the rationale for the selected balance of variants associated with common disease, rare disease, uncharacterized variants and variants not yet observed in nature
- If appropriate, explain the rationale for the selected balance of elements that harbor candidate disease association variants, candidate regulatory elements for disease-associated genes, or uncharacterized candidate regulatory elements
- Describe considerations for balancing testing capacity with obtaining a systematic sampling of variants and/or elements
- As the strategy will be decided by the consortium during the first year (see below), applicants should indicate how they could revise their plan to take into account the consortium strategy.

Application of genomic perturbation methods to assay the impact of interactions on phenotypes

Applicants must propose a plan to apply genomic perturbation methods to collect high quality phenotypic data using one or more robust assays, and to analyze that data.

This plan should:

- Describe how high-throughput perturbations will be performed, starting by the end of the first year
- Describe how high-throughput phenotype data will be collected, starting by the end of the first year
- Describe how data will be processed and analyzed, including applying the framework to assess interaction strength, starting by the end of the first year
- Explain the rationale for the choice of assay(s) in relation to the variants/elements, interactions, and phenotypes being considered
- Explain the rationale for the proposed balance between the number of samples versus the number of assays per sample (if using more than one assay)
- Explain the rationale for the biological system(s) used, including the relevance of that system to human health and disease
- Explain rationale for the choice of phenotype(s) used as experimental observables
- Explain rationale for balancing throughput and biological relevance
- Explain how the methods, approach or results could generalize to be applicable beyond the chosen variants, samples or biological systems
- Describe how high-quality samples with consents appropriate to project will be obtained. NHGRI expects that all human data generated by this NHGRI-funded research project will be derived from specimens or cell lines for which explicit consent for future research use and broad data sharing can be documented ([NOT-HG-20-011](https://grants.nih.gov/grants/guide/notice-files/NOT-HG-20-011.html) (<https://grants.nih.gov/grants/guide/notice-files/NOT-HG-20-011.html>)). Sources with participant consent for **unrestricted access** are strongly encouraged. Sources consented for General Research Use (GRU) or Health, Medical, and Biomedical (HMB) through a controlled-access environment may also be considered but need to be well justified. Studies should include samples that are derived from individuals of diverse ancestry and allow for consideration of sex as a biological variable
- Explain how using innovative methods and analyses will be balanced with the ability to reliably deliver large amounts of useful data and analyses to the community'
- Describe how the results of tested variant combinations will be displayed in the IGVF catalog and accessed by the community.

Model for prioritizing interaction testing (optional)

Applicants may propose a plan to generate a model for prioritizing future interaction combinations that are likely to be enriched in effects beyond additive. However, this may not be possible for some experimental approaches.

This plan should:

- Describe how the model will be generated, including inputs and outputs
- Describe how results from testing joint effects will be used
- The model need not be machine learning or artificial intelligence (ML/AI); it could even be simple heuristics (examples include, but are not limited to, ideas such as whether the variants are in the same pathway, or whether the variants are in paralogous genes, or whether the variants reside in genes in the same complex, or whether the variants reside in genes functioning in different cell types)
- Describe how the models for predicting the most informative combinations to test as part of the IGVF catalog.

Contribute results of tested variant combinations as well as models for predicting the most important combinations to test as part of the IGVF catalog.

Applicants must present a plan to incorporate results, including data and models, into a consortium-wide catalog relating variants/elements to phenotypes. This proposed plan must indicate how the catalog would allow the community to interpret the results obtained. Ultimately the consortium will generate a single catalog, rather than each project developing their own catalog. This catalog will be developed collaboratively by the consortium and hosted by the DACC. The implemented plan will be selected by the consortium during the first year, and thus may not match the plan proposed by any applicant.

This plan should:

- Describe plans for submitting raw data, processed data, and metadata to the DACC starting with the first year of the project
- Describe plans for working with the DACC to implement a data model and specify use cases appropriate to the center's data types and analyses during the first year of the project
- Describe the information to be reported in the catalog
- Describe how the information could be presented in the catalog
- Describe how concordant and discordant data will be presented and interpreted, as well as sparse data
- Describe the use cases for the external community that would be supported by these elements of catalog
- Describe plans for employing best practices and state of the art technology, including where appropriate, emphasis on data interoperability and scalability of tools, software, and approaches
- Indicate how they would work with the consortium to achieve consensus for a single catalog, and how they will revise their plan to take into account the consortium strategy

Enable others to perform related studies using these approaches

Applicants must describe their plan to enable others in the field to adopt the approaches used by this project and the consortium.

This plan should:

- Provide a high-level description of rapidly sharing of data and results (details should be in the Data Management and Sharing Plan/DMSP).
- Provide a high-level description of rapidly sharing resources, such as algorithms, software, protocols, plasmids, reporter or guide RNA sequences, models and file formats (details should be in the Resource Sharing plan).

Improvements in generalizable approaches or technologies for high-throughput interaction assays (optional).

Applicants have the option to propose to use a small portion of their resources to develop and/or refine experimental and/or computational approaches. However, this is NOT a technology development funding opportunity, and the center CANNOT be dependent upon the success of this activity.

If included, this plan should:

- Explain the potential to implement the technology during the current project period
- Explain how the technology might complement or replace other methods proposed for the project
- Describe the expected improvement (throughput, sensitivity, specificity, improved compatibility across biological systems, etc.)
- Describe the throughput and generalizability of the technology across experimental systems and diseases
- Describe the potential for other groups to adopt the technology, either within the consortium or the external community
- Not exceed 5% of the awarded budget.

Resource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

The following instructions also apply:

The Resource Sharing Plan should summarize whether and how resources (e.g., educational materials; methods; models; physical products, materials, and reagents; protocols; research findings and products; and software) will be made available. Applicants should include a description of the format, an indication of who will be responsible for implementation and plans for long-term maintenance, whether there will be opportunities for community input and feedback, platform(s) or mechanism(s) that will be used to make resources publicly accessible, and proposed timeline for implementing the Resource Sharing Plan. Resource Sharing Plans should not duplicate other sections of the main Research Plan but should refer to them when appropriate. After initial review, NHGRI program staff may negotiate revisions of this plan with the prospective awardee. The final negotiated version of this plan will become a term and condition of the award.

In addition to the above expectations, NHGRI expects that plans for sharing software generated under this funding opportunity will meet the following expectations:

- Applicants sharing software are encouraged to consider the NIH Best Practices for Sharing Research Software and the Findable, Accessible, Interoperable and Reusable Principles for Research Software (FAIR4RS) Principles, and to use software licenses that allow for unrestricted redistribution and modification of the software.
- Source code should be freely available to biomedical researchers and educators in the non-profit sector, such as institutions of education, research institutions, and government laboratories. The terms of software availability should permit the commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages.
- NHGRI encourages making software citable with persistent identifiers such as a DOI or a citation.cff.
- To preserve utility to the community, the software should be transferable such that another individual or team can continue development if the original investigators are unable to do so.
- Software should be containerized and promote reproducibility and use of automated pipelines, where possible. Developed software are expected to be tested utilizing a relevant testing framework where appropriate (e.g., unittest).
- Applicants should take responsibility for creating the original and subsequent "official" versions of a piece of software.

For more guidance on writing a Resource Sharing Plan, see <https://www.genome.gov/about-nhgri/Policies-Guidance/Writing-a-Resource-Sharing-Plan> (<https://www.genome.gov/about-nhgri/Policies-Guidance/Writing-a-Resource-Sharing-Plan>).

Other Plan(s):

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed, with the following additional instructions:

- A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page \(https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page\)](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.
- Recipients must comply with the NIH Genomic Data Sharing Policy ([NIHGPS 8.2.3.3 \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.2.3_sharing_research_resources.htm?#Genomic\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.2.3_sharing_research_resources.htm?#Genomic)).
- All scientific data, metadata, and predictions should be submitted to the IGVF Data Portal. The IGVF DACC will be responsible for additional deposition into appropriate NIH-designated repositories.

Appendix: Only limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400).

- No publications or other material, with the exception of blank questionnaires or blank surveys, may be included in the Appendix.

PHS Human Subjects and Clinical Trials Information

When involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research experience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400), with the following additional instructions:

If you answered "Yes" to the question "Are Human Subjects Involved?" on the R&R Other Project Information form, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** record.

Study Record: PHS Human Subjects and Clinical Trials Information

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

Delayed Onset Study

Note: [Delayed onset \(https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy\)](https://grants.nih.gov/grants/glossary.htm#DelayedOnsetStudy) does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

PHS Assignment Request Form

All instructions in the [How to Apply - Application Guide \(https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/url_redirect.htm?id=82400) must be followed.

Foreign Organizations

Foreign (non-U.S.) organizations must follow policies described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11137\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11137), and procedures for foreign organizations described throughout the How to Apply Application Guide.

3. Unique Entity Identifier and System for Award Management (SAM)

See Part 2. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active registrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, and Grants.gov

4. Submission Dates and Times

Part I. contains information about Key Dates and times. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date falls on a weekend or [Federal holiday \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82380\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82380), the application deadline is automatically extended to the next business day.

Organizations must submit applications to [Grants.gov \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11128\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11128) (the online portal to find and apply for grants across all Federal agencies). Applicants must then complete the submission process by tracking the status of the application in the [eRA Commons \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123), NIH's electronic system for grants administration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be corrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a Changed/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and time are subjected to the [NIH Grants Policy Statement Section 2.3.9.2 Electronically Submitted Applications \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82423).

Applicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

Information on the submission process and a definition of on-time submission are provided in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400).

5. Intergovernmental Review (E.O. 12372)

This initiative is not subject to [intergovernmental review. \(https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_10/10.10.1_executive_orders.htm)

6. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120).

Pre-award costs are allowable only as described in the [NIH Grants Policy Statement Section 7.9.1 Selected Items of Cost \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11143\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11143).

7. Other Submission Requirements and Information

Applications must be submitted electronically following the instructions described in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400). Paper applications will not be accepted.

Applicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about registration.

For assistance with your electronic application or for more information on the electronic submission process, visit [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400). If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the [Dealing with System Issues \(https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm\)](https://grants.nih.gov/grants/how-to-apply-application-guide/due-dates-and-submission-policies/dealing-with-system-issues.htm) guidance. For assistance with application submission, contact the Application Submission Contacts in Section VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile form. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this NOFO for information on registration requirements.

The applicant organization must ensure that the unique entity identifier provided on the application is the same identifier used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the [How to Apply – Application Guide \(https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400\)](https://grants.nih.gov/grants/guide/uri_redirect.htm?id=82400).

See [more tips \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11146\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11146) for avoiding common errors.

Upon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and responsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not be reviewed.

Mandatory Disclosure

Recipients or subrecipients must submit any information related to violations of federal criminal law involving fraud, bribery, or gratuity violations potentially affecting the federal award. See Mandatory Disclosures, [2 CFR 200.113 \(https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113\)](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200/subpart-B/section-200.113) and [NIH Grants Policy Statement Section 4.1.36 \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4.1.36_mandatory_disclosures.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4.1.36_mandatory_disclosures.htm).

Send written disclosures to the NIH Chief Grants Management Officer listed on the Notice of Award for the IC that funded the award and to the [HHS Office of Inspector Grant Self Disclosure Program \(https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/\)](https://oig.hhs.gov/compliance/self-disclosure-info/hhs-oig-grant-self-disclosure-program/) at [grantdisclosures@oig.hhs.gov \(mailto:grantdisclosures@oig.hhs.gov\)](mailto:grantdisclosures@oig.hhs.gov).

Post Submission Materials

Applicants are required to follow the instructions for post-submission materials, as described in [the policy \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82299\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82299)

Section V. Application Review Information

1. Criteria

Only the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the [NIH mission \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11149\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11149) are evaluated for scientific and technical merit through the NIH peer review system.

Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the review criteria below in the determination of scientific merit and give a separate score for each. 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.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Specific to this NOFO:

- To what extent will the proposed project contribute to the consortium goals of assessing the impact of genomic variation on genome function and phenotype?
- To what extent will the proposed project contribute to learning how best to do future studies of variant interactions?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? 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?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

Specific to this NOFO:

- To what extent does the proposed approach provide a plan that will achieve the stated NOFO objectives:
 - Propose a theoretical and quantitative framework for assessing interactions?
 - Apply the proposed framework to characterize interactions?
 - Contribute results of tested variant combinations as well as models (if any) for predicting the most important combinations to test as part of the IGVF catalog?
 - Enable others to perform related studies using these approaches?
- To what extent are the proposed assay(s) high-throughput, cost-effective and state-of-the-art, and capable of producing high quality data from the first year of the project?
- To what extent is the informatics infrastructure described adequate to support proposed analyses, and data deposition requirements from the first year of the project?
- To what extent are the milestones, timelines and goals proposed for the research project reasonable and realistic?
- To what extent does the proposed approach include elements that will enable others to perform related studies using these approaches?
- To what extent is the approach generalizable to diseases and biological processes other than those proposed?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment, and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

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.

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 research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the [Guidelines for the Review of Human Subjects \(http://grants.nih.gov/grants/guide/redirect.htm?id=11175\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11175).

This NOFO only accepts applications that do not propose clinical trials. Note: Applications may propose activities involving human subjects that are not deemed clinical trials.

Inclusion of Human Subjects Policies

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for inclusion. For additional information on review of the Inclusion section, please refer to the [Guidelines for the Review of Inclusion in Clinical Research \(http://grants.nih.gov/grants/guide/redirect.htm?id=11174\)](http://grants.nih.gov/grants/guide/redirect.htm?id=11174).

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following three points: (1) a complete description of all proposed procedures including the species, strains, ages, sex, and total numbers of animals to be used; (2) justifications that the species is appropriate for the proposed research and why the research goals cannot be accomplished using an alternative non-animal model; and (3) interventions including analgesia, anesthesia, sedation, palliative care, and humane endpoints that will be used to limit any unavoidable discomfort, distress, pain and injury in the conduct of scientifically valuable research. Methods of euthanasia and justification for selected methods, if NOT consistent with the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals, is also required but is found in a separate section of the application. For additional information on review of the Vertebrate Animals Section, please refer to the [Worksheet for Review of the Vertebrate Animals Section](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11150). (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11150)

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.

Resubmissions

For Resubmissions (as applicable), the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewals

For Renewals (as applicable), the committee will consider the progress made in the last funding period.

Revisions

For Revisions (as applicable), the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

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.

Applications from Foreign Organizations

Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

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 Resource Sharing Plan(s) (e.g., [Sharing Model Organisms \(https://sharing.nih.gov/other-sharing-policies/model-organism-sharing-policy#policy-overview\)](https://sharing.nih.gov/other-sharing-policies/model-organism-sharing-policy#policy-overview)) or the rationale for not sharing the resources, is reasonable.

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.

2. Review and Selection Process

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by CSR, in accordance with [NIH peer review policies and practices \(http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11154\)](http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11154), using the stated review criteria. Assignment to a Scientific Review Group will be shown in the eRA Commons.

As part of the scientific peer review, all applications will receive a written critique.

Applications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.

[Requests for reconsideration of initial peer review \(https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.4.2_appeals_of_initial_scientific_review.htm\)](https://grants.nih.gov/grants/policy/nihgps/html5/section_2/2.4.2_appeals_of_initial_scientific_review.htm) will not be accepted for applications submitted in response to this NOFO.

Applications will be assigned to NHGRI. Applications will compete for available funds with all other recommended applications submitted in response to this NOFO. Following initial peer review, recommended applications will receive a second level of review by The National Advisory Council for Human Genome Research. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Synergy with other IGTV funded projects and programmatic balance, including a variety of experimental assays, throughput and capacity of the approaches

- Potential to work effectively in large collaborative efforts or research consortia
- Adequacy of data sharing, software and analysis sharing and resource sharing plans as determined by NHGRI program staff
- Expansion of the community of genomic science to include new investigators and experienced investigators who are new to this field
- Inclusion of new investigators and experienced investigators that are new to NHGRI consortia
- Whether an applicant will be funded as a PD/PI through the other NOFOs in the IGVF Consortium to encourage participation from a broader representation of the research community

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the [NIH Grants Policy Statement Section 2.5.1. Just-in-Time Procedures](#) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82418). This request is not a Notice of Award nor should it be construed to be an indicator of possible funding.

Prior to making an award, NIH reviews an applicant's federal award history in SAM.gov to ensure sound business practices. An applicant can review and comment on any information in the Responsibility/Qualification records available in SAM.gov. NIH will consider any comments by the applicant in the Responsibility/Qualification records in SAM.gov to ascertain the applicant's integrity, business ethics, and performance record of managing Federal awards per 2 CFR Part 200.206 "Federal awarding agency review of risk posed by applicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

3. Anticipated Announcement and Award Dates

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the [eRA Commons](#) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11123). Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

Information regarding the disposition of applications is available in the [NIH Grants Policy Statement Section 2.4.4 Disposition of Applications](#) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=82416).

Section VI. Award Administration Information

1. Award Notices

A Notice of Award (NoA) is the official authorizing document notifying the applicant that an award has been made and that funds may be requested from the designated HHS payment system or office. The NoA is signed by the Grants Management Officer and emailed to the recipient's business official.

In accepting the award, the recipient agrees that any activities under the award are subject to all provisions currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the time of the award, and applicable statutory provisions.

Recipients must comply with any funding restrictions described in Section IV.6. Funding Restrictions. Any pre-award costs incurred before receipt of the NoA are at the applicant's own risk. For more information on the Notice of Award, please refer to the [NIH Grants Policy Statement Section 5. The Notice of Award](#) (https://grants.nih.gov/grants/policy/nihgps/HTML5/section_5/5_the_notice_of_award.htm) and NIH Grants & Funding website, see [Award Process](#). (<https://grants.nih.gov/grants/pre-award-process.htm#award>)

Institutional Review Board or Independent Ethics Committee Approval: Recipient institutions must ensure that protocols are reviewed by their IRB or IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the recipient must provide NIH copies of documents related to all major changes in the status of ongoing protocols.

2. Administrative and National Policy Requirements

The following Federal wide and HHS-specific policy requirements apply to awards funded through NIH:

- The rules listed at [2 CFR Part 200](#) (<https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200>), Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards.
- All NIH grant and cooperative agreement awards include the [NIH Grants Policy Statement](#) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11120) as part of the terms and conditions in the Notice of Award (NoA). The NoA includes the requirements of this NOFO. For these terms of award, see the [NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General](#) (https://grants.nih.gov/grants/policy/nihgps/HTML5/part_ii_terms_and_conditions_of_nih_grant_awards.htm) and [Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Recipients, and Activities](#) (http://grants.nih.gov/grants/guide/uri_redirect.htm?id=11159).

All federal statutes and regulations relevant to federal financial assistance, including those highlighted in [NIH Grants Policy Statement Section 4 Public Policy Requirements, Objectives and Other Appropriation Mandates](#). (https://grants.nih.gov/grants/policy/nihgps/HTML5/section_4/4_public_policy_requirements_objectives_and_other_appropriation_mandates.htm)

By applying for or accepting federal funds from HHS, recipients certify compliance with all federal antidiscrimination laws and these requirements and that complying with those laws is a material condition of receiving federal funding streams. Recipients are responsible for ensuring subrecipients, contractors, and partners also comply.

Applicants and recipients are strongly encouraged to refer to the [NIH Director's Statement of Priorities](#) (<https://www.nih.gov/about-nih/nih-director/statements/advancing-nih-mission-through-unified-strategy>), entitled "Advancing NIH's Mission Through a Unified Strategy."

Recipients are responsible for ensuring that their activities comply with all applicable federal regulations. Pursuant to 2 CFR 200.340, by accepting an NIH award, the recipient agrees that continued funding for the award is contingent upon the availability of appropriated funds, recipient satisfactory performance, compliance with the Terms and Conditions of the award, and may also otherwise be terminated, to the extent authorized by law, if the agency determines that the award no longer effectuates the program goals or agency priorities, in line with 2 CFR 200.340(a)(4).

Pursuant to the Cybersecurity Act of 2015, Div. N, § 405, Pub. Law 114-113, 6 USC § 1533(d), the HHS Secretary has established a common set of voluntary, consensus-based, and industry-led guidelines, best practices, methodologies, procedures, and processes.

Successful recipients under this NOFO agree that:

When recipients, subrecipients, or third-party entities have:

- ongoing and consistent access to HHS owned or operated information or operational technology systems; and
- receive, maintain, transmit, store, access, exchange, process, or utilize personal identifiable information (PII) or personal health information (PHI) obtained from the awarding HHS agency for the purposes of executing the award.

Cybersecurity plans and procedures **must** at minimum include the following:

- Develop cybersecurity plans and procedures, modeled after the [NIST Cybersecurity framework](#) (<https://www.nist.gov/cyberframework>), to protect HHS systems and data:
 - **Identify:**
 - Develop an inventory of all assets and accounts with access to HHS owned and operated information or operational technology systems or which obtain PII or PHI for the purposes of the award.
 - **Protect:**
 - Limit access to HHS owned and operated systems to only those in need of access to complete reward activities.

- Require all staff to complete annual cybersecurity and privacy awareness training. Visit [405\(d\): Knowledge on Demand \(hhs.gov\)](https://405d.hhs.gov/kod/five-threats) (<https://405d.hhs.gov/kod/five-threats>) to obtain free trainings, if needed.
- Enable multifactor authentication for all employees, subrecipients, and third-party entities to access HHS owned and operated information or operational technology systems.
- Regularly backup sensitive data and test backups.
- **Detect:**
 - Install anti-virus or anti-malware software on all devices, servers, and accounts used to connect to HHS owned and operated systems.
- **Respond:**
 - Develop an incident response plan. See [Incident-Response-Plan-Basics_508c.pdf \(cisa.gov\)](https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf) (https://www.cisa.gov/sites/default/files/publications/Incident-Response-Plan-Basics_508c.pdf) to learn about developing incident response plans.
 - Have cybersecurity incident reporting procedures that ensure the relevant HHS awarding agencies are notified of a cybersecurity incident within 48 hours of discovery. A cybersecurity incident is defined as an unplanned interruption to a technology service or reduction in the quality of a technology service, or an occurrence that actually or potentially jeopardizes the confidentiality, integrity, or availability of an information system or the information the system processes, stores, or transmits.
- **Recover:**
 - Investigate incidents and plug any security gaps identified.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate; racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

For applications involving substance abuse, the application must not support harm reduction. Please see [Updated Funding Guidance for Recipients on Supplies and Services](https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf) (<https://www.samhsa.gov/sites/default/files/dear-colleague-letter-updated-hr-funding-guidance.pdf>).

For applications involving funding Medication-Assisted Treatment (MAT) or medications for opioid use disorder (MOUD), this funding should be used to provide comprehensive treatment and recovery support services rather than medication-only models for opioid use disorder. Services should include medications, where clinically indicated, in conjunction with psychosocial and other treatment and recovery support services. Funding can also be used to support individualized tapering and discontinuation of medications when clinically indicated. Please see [Updated Funding Guidance for Recipients on MAT/MOUD](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.samhsa.gov%2Fsites%2Fdefault%2Ffiles%2Fdear-colleague-letter-mat-moud-guidance.pdf&data=05%7C02%7Cchelsey.hughes%40nih.gov%7C725bb62d21f94a2b9ff908dec0bc5a25%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63916011238415) (<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.samhsa.gov%2Fsites%2Fdefault%2Ffiles%2Fdear-colleague-letter-mat-moud-guidance.pdf&data=05%7C02%7Cchelsey.hughes%40nih.gov%7C725bb62d21f94a2b9ff908dec0bc5a25%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63916011238415>).

As of October 1, 2025, HHS has adopted [2 CFR Part 200](https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200) (<https://www.ecfr.gov/current/title-2/subtitle-A/chapter-II/part-200>), with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75. However, for NIH, under the Consolidated Appropriations Act for FY 2026, ([P.L. 119-75](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.congress.gov%2Fbill%2F119th-congress%2Fhouse-bill%2F148&data=05%7C02%7Cantoine.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982) (<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.congress.gov%2Fbill%2F119th-congress%2Fhouse-bill%2F148&data=05%7C02%7Cantoine.caliman%40nih.gov%7C68a8e1e3db804c61b38f08deb0e88127%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C63914270982>)), the provisions relating to indirect costs in 45 CFR 75 continue to apply to NIH awards. Consistent with the statute, NIH will not apply updated thresholds outlined within 2 CFR Part 200, at this time.

In administering programs under this and all funding announcements, NIH prioritizes:

- Research involving rigorous scientific methods, including for studies related to children and adolescents, where NIH is committed to approaches that reflect the highest standards of clinical care and child safety.
- Biological and physiological integrity: Recognizing the relevance of biological sex to health outcomes, NIH encourages applicants to account for sex-based health factors in program design, data collection, and service delivery where scientifically appropriate.
- NIH will implement these priorities consistent with applicable laws, regulations, court orders, and all required administrative procedures. Applicants are encouraged to describe how their proposed programs align with these priorities in their project narratives. Funded activities must advance NIH's vision of protecting and improving the health and well-being of Americans. The particular focus is on those who are medically vulnerable, or live in areas with limited access to care. NIH's duty is to serve wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (HHS) grant administration regulations at 2 CFR Part 200, and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the recipients is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the recipients for the project as a whole, although specific tasks and activities may be shared among the recipients and NIH as defined below.

The PD(s)/PI(s) will have the primary responsibility for:

- Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.
- Determining research approaches, designing protocols, setting project milestones and timelines, and conducting research.
- Ensuring that the software, resources, materials, etc. produced as part of this project are released appropriately according to the Resource Sharing Plan, IGVF Consortium policies, and NIH policies.
- Ensuring that the data produced as part of this project are released appropriately according to the Data Management and Sharing Plan, IGVF Consortium policies, and NIH policies.
- Adhering to policies regarding sharing of genomic and other types of data, data access, and standardized formats; timely publication; and intellectual property established by the NIH, NHGRI, and the Steering Committee (SC).
- Not disclosing confidential information.
- Interacting with other relevant NHGRI and NIH activities to promote synergy and consistency among similar or related projects.
- The PD/PI and his/her staff will be required to fully participate with NIH staff, External Scientific Consultants (upon NHGRI request), IGVF Consortium investigators, and one another. This includes collaborating with other projects and consortia, such as the Atlas of Variant Effects (AVE) Alliance, the Molecular Phenotypes of Null Alleles in Cells (MorPhIC), the Clinical Genome (ClinGen) Resource, the Genomics Research to Elucidate the Genetics of Rare Diseases (GREGoR), the Human Pangenome Reference Consortium (HPRC), and others.
- Serve as a member of the IGVF Consortium Steering Committee (SC).
- Attending and participating in SC and other working group meetings and accepting and implementing decisions made by the SC.

- Collaborating with the Data and Coordinating Center (DACC). Recipients that are part of a consortium will work collaboratively with a DACC that is tasked with a variety of roles, such as: ensuring that the products are the highest quality; developing standards; disseminating information; providing logistics, outreach and training, etc. In order for the collaboration to be effective, PDs/PIs are responsible for:
 - Ensuring that the recipient receives the appropriate approvals for sharing data between the DACC and selected data repositories such as AnVIL, dbGaP, GEO, or ClinVar and other appropriate databases approved by the consortium and NHGRI.
 - Transferring, in a timely manner, of detailed (sequence, variant, other genomic, functional, phenotypic, , etc.) and related data and metadata, as appropriate, to the DACC, using agreed-upon formats and processes, to facilitate dissemination of data more broadly through databases such as AnVIL, dbGaP, GEO or ClinVar, and other appropriate databases.
 - Collaborating with the DACC to establish data formats and standards, to track and document collaborations and incoming samples, report findings, etc.
 - Fully disclosing data, analyses, algorithms, software source code, and experimental methods to the other members of the consortium for the purpose of scientific evaluation and use by other consortium members.
 - Collaborating with the DACC to track and document collaborations and incoming samples, report findings, etc. in a FAIR (Findable, Accessible, Interoperable, Reusable) manner.
 - Submitting periodic progress reports in a standard format, including metrics of the use and impact on the community, agreed on with the NHGRI Project Scientist/Scientific Officer (PS/SO).
 - Providing reports, summary statistics, and data, as appropriate, in a timely fashion as agreed upon by the PS/SO.
 - Sharing research resources, tools, and data with members of the consortium consistent with achieving the goals of the project.
 - Assess and disseminate data, protocols, consent materials, methods, analyses, models, model parameters, research resources, software, and tools developed for or derived from the DACC within and outside the consortium, as appropriate and according to the release policies developed for and by this project.
 - Abiding by common definitions, protocols, and procedures.

Recipients will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies. NIH will have unrestricted cost-free access and use of the data, resources and software generated by the recipient, including the right to transfer said data and/or software to other NIH-funded and/or managed resource projects, at the NIH's sole reasonable discretion upon termination or expiration of this award.

NIH staff have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

The Project Scientist/Scientific Officer (PS/SO) at NHGRI is a dual role held by a NHGRI Program Director. In the Project Scientist role, the Program Director will have substantial scientific and programmatic involvement during the conduct of this activity through technical assistance, advice, and coordination. In the Scientific Officer role, the Program Director will be responsible for the normal scientific and programmatic stewardship of the award and manages concerns about bias as it affects the project. The role of NHGRI PS/SO will be to facilitate and not to direct the activities. The PS/SO will be named in the Notice of Award.

The PS/SO will have the following substantial involvement:

Serving as a liaison, helping to coordinate activities among and for the recipients, including acting as a liaison to the NHGRI and as an information resource for the recipients about genome research activities. The PS/SO will also coordinate the efforts of the recipient(s) with other groups conducting similar studies.

- Reporting periodically on the progress of the recipients to the NHGRI Director and to the National Advisory Council for Human Genome Research.
- Assisting recipient(s) in the development, if needed, of policies for dealing with situations that require coordinated action.
- Providing advice on the management and technical performance of the award.
- Assisting in promoting the availability of the data and related resources developed in the course of the award to the scientific community.
- Being responsible for the normal scientific and programmatic stewardship of the award, including assessments of how well the recipient has met any milestones required for each year of funding.
- Curtailing, withholding or reducing support for any recipient that fails to make sufficient progress toward the work scope that NHGRI approved, has ethical or conflict of interest issues, or fails to comply with the Terms and Conditions of Award.
- Involving NIH or NHGRI staff who may assist the recipient(s) as designated by the PS/SO.
- Participate in data analyses, interpretations, and, where warranted, co-authorship of the publication of results of studies conducted through the IGVF Consortium.
- Negotiate milestones, e.g., throughput, quality, and biological samples with the recipients, as necessary.
- Participate with the other SC members in the group process of setting research priorities, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted.

External Scientific Consultants (ESC): The NHGRI PS/SO may engage external scientists with relevant scientific and consortium experience, who are not funded as part of the project and who agree to a confidentiality policy, to provide input and advice to the NHGRI PS/SO about the project. The PS/PO will appoint scientists to the ESC and will determine the durations of service. Activities of the ESC could include:

- Participating, as appropriate, in consortium meetings, Steering Committees calls, and the annual recipients' meetings; a subset of ESC members may also meet remotely at other times during the project period, as needed.
- Reviewing and evaluating the progress of recipients (individually or as a group) in achieving the goals of the project.
- Recommending changes in priorities based on scientific advances within and outside the consortium.
- Providing individual recommendations regarding any changes in the project or grant(s) as necessary.

The PS/SO will consider recommendations from individual ESCs to recommend project changes to the PD/PI, as appropriate.

Areas of Joint Responsibility include:

As there are multiple awards working toward a common goal, close interaction between the participating recipient(s) and the PS/SO will be required, to manage, assess, and implement activities towards the common goals of the consortium. This is accomplished by:

- Meeting monthly for conference calls to share information on data resources, methodologies, analytical tools, data analyses, preliminary results, etc.
- Establishing best practices for data integration and collaborative analyses as appropriate.
- Setting research priorities, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted.
- Generating responses to ESC recommendations.

The PS/SO will assist and facilitate the group process and not direct it.

- Steering Committee (SC): The SC will be the main governing body of the Consortium. The purpose of the SC will be to recommend directions for a consortium consistent with achieving the project goals, develop consortium policies to build synergy and improve communication and collaboration between the projects, and to provide a forum for discussing progress, challenges and opportunities for the consortium.
- The SC will convene for monthly conference calls and yearly in-person meetings in the first two years, and monthly conference calls and one time per year in-person meetings in years 3-5 to share information on data resources, methodologies, analytical tools, data analyses, preliminary results, etc. As needed, additional meetings of the SC, working

groups and consortium members will be determined by the SC.

- The SC will be composed of one representative from each of the grants awarded in the consortium. Each PD/PI will decide who will be its representative. Multi-PI grants will have one representative. Each representative will have one vote; The PS/SO will be a voting member. Other designated NIH staff, External Scientific Consultants, or other designated participants may attend the SC meetings on a regular or ad-hoc basis, but will be ex officio (non-voting) members.
- The SC will develop its own operating procedures.
- The SC may establish subcommittees or working groups to oversee the development and implementation of consortium policies including data and software releases, publications and standards, etc. Subcommittees or working groups may be either permanent or time limited, may include additional experts, depending on the needs of the research.
- The PD(s)/PI(s) will be expected to play an active role in these working groups, as appropriate.
- It is expected that most of the decisions on the activities of the SC will be reached by consensus. If a vote is needed, at least 60% of the voting members must vote in favor of the proposal.
- NIH staff will review and approve policies developed by the SC.
- Recipients will be required to accept and implement policies approved by the SC.

Dispute Resolution:

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and NHGRI may be addressed by convening a Dispute Resolution Panel. It will be composed of three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of disagreement for one award, the first member may be chosen by that recipient. This special dispute resolution procedure does not alter the recipient's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and HHS regulation 45 CFR Part 16.

3. Data Management and Sharing

A Data Management and Sharing Plan (DMS Plan) is required for any NIH-funded or conducted research that will generate scientific data. Applicants must submit the DMS Plan at the time of application using the [NIH DMS Plan Format Page \(https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page\)](https://grants.nih.gov/grants-process/write-application/forms-directory/data-management-and-sharing-plan-format-page). The DMS Plan must address the elements in the structured format. Where the DMS Plan Format Page requires a "Yes or No" response, no additional narrative is allowed.

4. Reporting

When multiple years are involved, recipients will be required to submit the [Research Performance Progress Report \(RPPR\) \(http://grants.nih.gov/grants/rppr/index.htm\)](http://grants.nih.gov/grants/rppr/index.htm) annually and financial statements as required in the [NIH Grants Policy Statement Section 8.4.1 Reporting. \(https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm\)](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_8/8.4.1_reporting.htm). To learn more about post-award monitoring and reporting, see the NIH Grants & Funding website, see [Post-Award Monitoring and Reporting \(https://grants.nih.gov/grants/guide/url_redirect.php?id=82428\)](https://grants.nih.gov/grants/guide/url_redirect.php?id=82428).

A final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as described in the [NIH Grants Policy Statement Section 8.6 Closeout \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=82420). NIH NOFOs outline intended research goals and objectives. Post award, NIH will review and measure performance based on the details and outcomes that are shared within the RPPR, as described at 2 CFR Part 200.301.

Section VII. Agency Contacts

We encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

Application Submission Contacts

[eRA Service Desk \(https://www.era.nih.gov/need-help\)](https://www.era.nih.gov/need-help) - Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that threaten submission by the due date, and post-submission issues.

[Grants.gov Support Center \(https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7CantoINETte.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b](https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fgrants.gov%2Fsupport&data=05%7C02%7CantoINETte.caliman%40nih.gov%7Caf6dde64d644478d4e8b08dde6700581%7C14b77578977342d58507251ca2dc2b)

- Questions regarding Grants.gov registration and services (e.g., Workspace, subscriptions).

Scientific/Research Contact(s)

IGVF Program Team

National Human Genome Research Institute (NHGRI)

Email: nhgri-igvf@mail.nih.gov (<mailto:nhgri-igvf@mail.nih.gov>)

Peer Review Contact(s)

Examine your eRA Commons account for review assignment and contact information (information appears two weeks after the submission due date).

Financial/Grants Management Contact(s)

Grants Administration Branch

National Human Genome Research Institute (NHGRI)

Email: nhgrigab@mail.nih.gov (<mailto:nhgrigab@mail.nih.gov>)

Section VIII. Other Information

Recently issued trans-NIH [policy notices \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11163) may affect your application submission. A full list of policy notices published by NIH is provided in the [NIH Guide for Grants and Contracts \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11164). All awards are subject to the terms and conditions, cost principles, and other considerations described in the [NIH Grants Policy Statement \(http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120\)](http://grants.nih.gov/grants/guide/url_redirect.htm?id=11120).

Authority and Regulations

Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 2 CFR Part 200.