A governance policy for partnership with external funding opportunities

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1 Document History

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1.1 Version History

Version	Date	Description
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1.2 Reviewers

This document must be reviewed by the following:

Name	Title	Version
Mark Caulfield	Chief Scientist	1.5
Tom Fowler	Deputy Chief Scientist & Director of Public Health	1.5
Nick Maltby	General Counsel and Company Secretary	1.5

1.3 Approvers

This document must be approved by the following:

Name	Responsibility	Date	Version
Mark Caulfield	Chief Scientist		1.5
Tom Fowler	Deputy Chief Scientist & Director of Public Health		1.5

Nick Maltby	General Counsel and Company Secretary		1.5

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2 A governance policy for partnership with external funding opportunities

2.1 Introduction and overview

This document outlines the Genomics England governance policy for the consideration of funding proposals for projects associated with the 100,000 Genomes Project and the work of Genomics England. This governance policy is for non-commercial partnerships and engagement only and aims to create a framework to engage in funding which enables researchers to make use of an infrastructure Genomics England has already built (with the corresponding benefit of economies of scale). **This policy does not outline the route for access to data by commercial organisations or researchers supported by commercial external funders.** Commercial access and engagement, including academic-led industry partnerships, must be via the GENE Consortium or other direct contractual arrangement with Genomics England. Regardless of the funding arrangement, academic researchers wishing to access Genomics England data are required to be part of a GeCIP Domain and work must be carried out in accordance with the GeCIP Rules.

This governance policy covers two key categories of engagement with external funding providers:

2.2 Category 1 funding

Researchers in the Genomics England Clinical Interpretation Partnership (GeCIP) will require external funding to undertake GeCIP work that falls within the current project remit (See Appendix 2), and may seek a letter of support from Genomics England. An example would be additional bioinformatics infrastructure or training fellowships to work on Genomics England data.

Genomics England cannot award grants to GeCIP domains. Instead, GeCIP domains have been asked to develop research plans that will be evaluated by Genomics England and will need to seek funds by application to GeCIP funders or other charitable funders. These applications will be subject to approval via the scientific peer review process of the respective GeCIP funders. For engagement that falls within category 1, Genomics England is not the decision-maker on the grant. Within this paper, we outline the criteria and process for issuing a letter of support. Genomics England will not within Category 1 support a funding application that does not comply with the GeCIP rules and falls outside of the Genomics England mission and the current project remit (see Appendix 1 and Appendix 2

for further details on the Genomics England mission and the 100,000 Genomes Project remit).

2.3 Category 2 funding

Funders and/or researchers may approach Genomics England seeking to form a partnership which falls outside the current remit and eligibility criteria of the project. This type of partnership will generally fall into one of two sub-categories:

a. A full direct cost-recovery arrangement, whereby Genomics England provides a range of negotiable services to an external organisation for a fee (for example, sample collection, sequencing and/or analysis for a disease that is currently out of scope). The fee will not cover overheads, as in the commercial space but not a return on investment. **This will be fully funded by the external organisation at no cost to Genomics England** and will involve partners such as NHS England where this exceeds current contractual requirements.
b. **Genomics England may consider waiving some costs for a project that is so closely aligned with Genomics England's core mission and current remit** but where the request reaches beyond the capability and capacity of Genomics England's current budget (for example, additional rare diseases, cancers or infectious disease where numbers requested or needed are beyond the current envelope of Genomics England). Where such additional projects meet this criterion and on the recommendation of the Science Advisory Committee and subject to Genomics England Board approval, a co-funding partnership may form between Genomics England and the third party funder. The Genomics England contribution may be, for example through the absorption of the costs of data infrastructure, where there is no additional cost for the activity. Genomics England will aim to recover any additional costs where they arise. Line items such as sequencing costs and annotation costs cannot be waived. Genomics England's contribution to any category 2 application will be in kind (access to the infrastructure) rather than cash.

The researchers involved in any successful **category 2** application will be required to join a GeCIP and all access will be provided through the GeCIP framework. **Genomics England will determine on a case by case basis whether it will be more appropriate for the researchers to join an existing GeCIP domain or whether to establish a new GeCIP domain.**

For both **category 1** and **category 2** applications, Genomics England expects that the researchers who have raised the research funds will lead the analysis of the relevant data in accordance with the GeCIP rules and regulations.

2.4 Types of external funding - Category 1 (within remit)

Types of external funding that may be available to GeCIP researchers for work that is within Category 1 include:

- Funding calls that explicitly fund research proposals that use the 100,000 Genomes Project dataset and contribute to the Genomics England Knowledge Base.
- Strategic initiatives initiated by GeCIP researchers which are directly targeted at enhancing clinical interpretation in partnership with Genomics England.
- Response mode funding from applications submitted to funders initiated by GeCIP researchers.
- Funding for training as part of the allied Health Education England programme or other trainee programmes related to the 100,000 Genomes Project.

While funding calls will be based on GeCIP funders' own priorities and assessment processes, we expect funding calls to drive collaborations between researchers, both nationally and internationally, as such collaborations are likely to result in stronger scientific researcher proposals.

Applications for funding to external funders will need to be registered with the Office of the Chief Scientist so Genomics England can manage competing demands fairly and equitably and ensure these accord with Genomics England's mission and ethical approvals.

Please see Appendix 3 for an example of a Category 1 (within remit) engagement.

2.5 Types of external funding - Category 2 (outside remit)

Additional activity occurring through a funding partnership mechanism (i.e. falling within category (2) above) could include the external-funding of additional sample and data collection in new or existing diseases. This could potentially (with NHSE agreement and change control procedure) be through the GMC infrastructure, with GMCs agreeing to undertake additional sample collection, or via separate agreements as is currently occurring with the CLL pilot project.

It would be expected that any such additional activity would still be covered by the 100,000 Genomes Project's general rules of engagement, i.e. such data would be held within the Genomics England data infrastructure, the same or agreed longitudinal requirements around data provision would apply, the same IP and publications policy would apply, and after a 6 month period of protected access (in accordance with the GeCIP rules) other researchers including GeCIP members could potentially request access. In certain circumstances, it may be necessary to adapt the standard requirements in accordance with ethical approvals, to allow additional scientific opportunities. This will require approval by the access review committee and subsequent recommendation.

Please see Appendix 4 for examples of Category 2 (outside remit) engagements.

2.6 Benefits of externally funded partnerships

Benefits will vary but could include:

- Access to GMC's recruitment structure (subject to the NHSE agreement and change-control procedure)
- Use of Genomics England data infrastructure and data centre
- Access to the available whole genome sequences and associated clinical data
- Access to a multi-omic sample repository
- Use of Genomics England analysis pipeline
- Project scale efficiencies e.g. agreed sequencing costs with Illumina
- Use of data collection infrastructure
- Opportunities for collaboration with Genomics England's network of researchers
- Inclusion of research data alongside other research initiatives e.g. clinical trials

2.7 Process for partnership with external funding opportunities

The following process should be followed for all engagement with external funders (including both category (1) and (2) above), however there may be cases where it is necessary to deviate from this guidance.

1. All external funding opportunities must be registered with the Office of the Chief Scientist.
2. A summary of the research proposal for which funding is required should be reviewed and approved by the scientific peer review process.
3. The following important questions should then be considered:
    a. Is there a reputation risk to the 100,000 Genomes Project or Genomics England?
    b. All applications should be considered in terms of the risk they could impose on Genomics England and the project as a whole. If a risk is imposed, any agreement to fund or letter of support from Genomics England should be subject to de-risking of the arrangement to the satisfaction of the Genomics England Board.
    c. Is it aligned with Genomics England's mission and ethical approvals?
    d. All applications should be considered in relation to how well they align with the Genomics England mission and ethical approvals. All such applications in category 1 and 2 will be assessed by the Genomics England Science Team and relevant cognate units within the Genomics England team. A summary and risk assessment will be produced for submission to the Science Advisory Committee

or other Advisory Committees as appropriate. The recommendations from this process will be taken to the Genomics England Board for consideration.

For **category 1** applications, Genomics England will support funding opportunities identified and initiated by GeCIP researchers that do not impose a reputation risk, align with the Genomics England mission and ethical approvals, and demonstrate collaboration and consultation with the relevant experts within GeCIP. A letter of support by Genomics England should be provided if required.

A **category 2(a)** application may still be considered even where it does not align with Genomics England's existing remit so long as it is fully costed and it meets the following criteria:

- It will bring benefit to patients;
- It will add to the premiere knowledge base for genomic medicine;
- Any risk to Genomics England or the project can be managed and are outweighed by the likely benefits of the partnership.

A **category 2(b)** application will need to meet all of the criteria set out above for a category 2(a) application, but for Genomics England to consider a partnership arrangement of this nature it **must also** be closely aligned with Genomics England's mission and current remit. We expect to develop a better understanding as to what falls within this category as applications are received.

All **category 2** applications will be discussed with Genomics England's core partners, including NHSE and the Department of Health, before any decision on the application is made (see below for the decision process).

The assessment of **category 2** applications must then follow the following procedure:

1. Before a formal decision on the application is made, applicants and Genomics England should confirm the type and conditions of engagement with the external partner.
2. Following all of the above steps and review by the Office of Chief Scientists, the Executive Chairman and the Scientific Advisory Committee, the Genomics England Board can approve or reject the partnership proposal.

3 Appendix 1

3.1 The Genomics England mission

The Project is designed to produce new capability and capacity for genomic medicine that will transform the NHS. It will also produce new capability for clinical genomics research. As part of the proposal a secure infrastructure has been established for the protection and analysis of clinical and genomic data. This will be made available for approved academic and industrial research purposes, including those of the contributing clinical organisations from the NHS.

Genomics England is working with research groups and funding organisations, to ensure that the new research capability will be fit for purpose and that the data is acquired and managed to appropriate standards. In addition, Genomics England, and its partners will ensure that the tools provided within the secure infrastructure will both accelerate scientific progress and support the focused, interdisciplinary collaboration needed for clinical interpretation and patient benefit. To maximise the value of this programme we have created the Genomics England Clinical Interpretation Partnership (GeCIP) which brings funders, researchers, NHS teams, trainees and potentially industrial partners together to enhance the value of this dataset for healthcare benefit.

We have developed this infrastructure with the opportunity to expand the Project to other diseases and approaches if separate funding is generated. In particular, our Medical Research Council-funded Data Infrastructure Award is designed to enhance the UK clinical research infrastructure in Genomic Medicine and could be used to store whole genome sequence from other disorders and a range of associated multi-omic datasets. Furthermore, our sequencing contract contains some elasticity to go beyond 100,000 whole genome sequences although we do not have funding for this additional activity at present.

3.2 The aims of the Project

The aims of the project are:

- Patient benefit: providing clinical diagnosis and in time, new or more effective treatments for NHS patients.
- New scientific insights and discovery: with the consent of patients, creating a database of 100,000 whole genome sequences linked to continually updated long term patient health and personal information for analysis by researchers.
- Accelerating the uptake of genomic medicine in the NHS: working with NHSE and other partners to deliver a scalable WGS and informatics platform to enable these

services to be made widely available for NHS patients. In addition, through the Genomics England Clinical Interpretation Partnership (GeCIP), creating a mechanism to both continually improve the accuracy and reliability of information fed back to patients and add to knowledge of the genetic basis of disease.

- Stimulating and enhancing UK industry and investment: by providing access to this unique data resource by industry for the purpose of developing new knowledge, methods of analysis, medicines, diagnostics and devices.
- Increasing public knowledge and support for genomic medicine: delivering an ethical and transparent programme which has public trust and confidence and working with a range of partners to increase knowledge of genomics.

4 Appendix 2

4.1 The 100,000 Genomes Project remit

Rare diseases, cancer and infectious diseases were selected as the focus for the 100,000 Genomes Project as they present high potential for significant health gain from this Project. Focus on these diseases offers the strongest prospect of patient and scientific benefits and the ability to drive the transformation of the NHS in terms of application of genomic medicine. Furthermore, given the current state of knowledge regarding the genetic architecture of these diseases, the application of WGS may enable major new biological insights that will enable new diagnostics and therapeutic innovation.

The rare disease strand of the 100,000 Genomes Project is intended to offer the opportunity for diagnosis and gene discovery in disorders or phenotypes for which there is likely to be a single gene basis for the phenotype in the patients recruited to the Project. The number of genomes afforded to any single phenotype will necessarily be limited and therefore we are unable to include large cohorts of any single specific phenotype. Accordingly, we are unable to include disorders for which the aetiology is likely to be complex and polygenic, as the size of cohort required for meaningful study of the genetic basis of such phenotypes will be beyond the scope of this program.

The cancer strand of the 100,000 Genomes Project is currently offering broad recruitment of primary tissue (surgical resections or biopsies) that have not undergone chemo, radio or hormonal therapy. The next step would be to recruit specific cohorts, defined by uniformity of tumour and/or patient characteristics and/or uniformity of treatment of patients.

Non-commercial researchers are required to become a GeCIP member in order to have access to the 100,000 Genomes Project data. A GeCIP researcher may be part of a disease-specific or function-specific domain which has been approved by the Genomics England Chief Scientist. In the case of a disease-specific domain, the researcher is undertaking research on the data pertaining to that disease as follows:

- undertake an ethically approved research project or equivalent work
- commit results/findings to the Genomics England Knowledge Base
- gain priority access to the relevant component of the 100,000 Genomes Project dataset via domain-specific embassy. No fee levied for data access

Genomics England cannot fund clinical trials but is generating capability to obtain fund from a third party to carry out such research.

6 Appendix 3

6.1 Example of a Category 1 (within remit) engagement

An interesting research variant arising in inherited cardiomyopathy has been verified. The variant of interest was found following whole genome sequencing of a cohort of cardiomyopathy samples recruited into the 100,000 Genomes Project Main Programme. The Cardiovascular Domain would like to perform further functional studies to assess the novel likely pathogenic variant using animal based disease models. This knowledge will add to the 100,000 Genomes Knowledge Base. The Cardiovascular Domain wish to apply for funding for funding for short-term research projects lasting up to three years and costing less than £300,000, in order to carry out these further studies. This study is within the project remit therefore, on review of the research proposal, Genomics England would contribute a letter of support towards the funding application made by the researchers.

7 Appendix 4

7.1 Example of a Category 2a (outside remit) full cost-recovery arrangement

The Endocrine and Metabolism domain would like to perform whole genome sequencing on a cohort of patients with type I diabetes of non-monogenic aetiology. Currently, only monogenic heritable rare disorders are eligible for recruitment into the 100,000 Genomes Project Main Programme and therefore, multifactorial/polygenic cases of type I diabetes are considered as being outside of the Project's remit. The researchers would be required to apply for 100% funding to support analysis of these genomes. However, the research would still need to be part of the GeCIP framework and the data would be required to be shared with researchers of the GeCIP domain. Genomics England will determine on a case by case basis whether it will be more appropriate for the researchers to join an existing GeCIP domain or whether to establish a new GeCIP domain. The research proposals would be reviewed by Genomics England and if appropriate the research may benefit from the agreed competitive rates in place between Genomics England and analytical pipeline partners (e.g. sequencing with Illumina).

7.2 Examples of Category 2b (outside remit) partnership arrangement

A large cohort of patients with familial breast cancer have already undergone whole exome sequencing in Study XYZ. Genomics England are also recruiting patients with familial breast

cancer and have confirmed a new variant and therefore researchers would like to go back to original cohort from Study XYZ and carry out whole genome sequencing in the same samples along with the new cohort of samples recruited to the 100,000 Genomes Project. The research team have plans further down the line to conduct omic analysis. This project closely aligns with the Genomics England mission, however, is beyond Genomics England capabilities therefore Genomics England may commit to funding a portion of this study in partnership with a third party funder.

The Haematological Oncology GeCIP has identified a new therapeutic agent targeting a novel pathway. The involved GeCIP domain clinicians would like to undertake a randomised trial testing the safety and efficacy of the intervention. The pharmaceutical company who own the drug donate the medicine but this is not an industry sponsored trial. Although Genomics England might be able to cover the cost of sequencing and capture of the phenotypic data, the cost of the development of the trial and the intervention would have to be funded by an external third party funder as these fall beyond the current project remit.