Genomics England Clinical Interpretation Partnership (GeCIP) Detailed Research Plan Form

Domain-wide sections

Application Summary	
GeCIP domain name	**Ethics and Social Science**
Project title *(max 150 characters)*	**Identification and analysis of practical ethical and social aspects of the clinical and research uses of genomics**

Objectives. *Set out the key objectives of your research. (max 200 words)*

The successful and appropriate conduct of genomics research and its effective translation into clinical genomics practice depend upon the establishment and maintenance of well-founded public trust and confidence. This in turn depends crucially upon the achievement of high ethical standards in research and in clinical practice. In these new and rapidly developing areas of medicine, existing models of clinical and research ethics are likely to require rethinking in the light of new challenges. The development of approaches to ethical practice capable of commanding the support of patients, the public, health professionals, and researchers requires ethical issues to be identified and analysed and for this analysis to inform the development of models of good practice. Rigorous social scientific research into the experiences, values, and concerns of patients, research participants, health professionals, researchers, and the wider public is essential to the development and evaluation of effective and appropriate genomic services and research.

Against this backdrop, the objectives of the Ethics and Social Science Domain are as follows:

- To conduct research on the ethical and societal aspects of the clinical and research uses of genomics
- To facilitate collaborative research partnerships bringing together researchers in ethics, the humanities, and social sciences with scientists across the GeCIP, health professionals, and patient groups.
- To play a co-ordinating role nationally encouraging collaboration between ethics and social science research groups currently conducting research across the GMS and the wider NHS.

Lay summary. *Information from this summary may be displayed on a public facing website. Provide a brief lay summary of your planned research. (max 200 words)*

The achievement of high ethical standards in medical research and clinical practice requires practical ethical, social and regulatory issues to be identified and analysed and for this work to inform the development of models of good practice. The Ethics and Social Science GeCIP domain will encourage and support research on the ethical aspects and social implications of the clinical and research uses of genomics in order to inform the development and implementation of high ethical standards. This work will have a particular focus on the work of the 100,000 Genomes Project and the NHS Genomic Medicine Service but will also look beyond this to the wider uses of genomics in the NHS in the future. It will aim to create collaborative research partnerships bringing together researchers in ethics, law and the social sciences with health professionals, patient groups, and scientists. In the first instance, the research conducted within the domain will cover research on: patient and participant experiences; ethical issues arising for health professionals and researchers in their practice; and, research on the analysis of key ethical concepts in the light of developments in genomics. This will be complemented by bespoke pieces of ethics and social science research embedded within other scientific and clinical GeCIP domains.

Technical summary. *Information from this summary may be displayed on a public facing website. Please include plans for methodology, including experimental design and expected outputs of the research. (max 500 words)*

The Ethics and Social Science Domain brings together researchers from a range of disciplinary backgrounds across the humanities and social sciences to conduct research on the ethical and social aspects of genomics research and clinical practice. Outputs will include: evidence regarding and analysis of practical ethical problems arising for health professionals and researchers; social scientific studies of patient and health professional experience; recommendations on good practice; and, the identification of areas requiring further research.

The current subdomains in the Ethics and Social Science GeCIP are:

- Ethics in Practice;
- Analysis of Key Ethical Concepts;
- Patient and Participant Experience (including two Health Education England Fellowship Projects already approved by the SAC and ARC)

Our aspiration is that additional sub-domains will be developed and incorporated into this Domain in the near future. The first of these are likely to focus on (i)law and regulation and (ii)diversity and health equity.

Sub-domain leads will develop and implement ethics and social science research projects addressing a range of ethical, social and regulatory questions. These sub-domains will be complementary and collaboration across them, and with researchers in other domains, will be strongly encouraged. Data requirements for the research undertaken in these sub-domains will differ significantly from that in other domains:

- Most of the research in this domain will not require access to any patient data at all. Examples of this might be an ethical analysis of different proposed approaches to additional findings, or research exploring the practical ethical issues arising in the day to day work of health professionals and/or scientists.
- In some cases, although researchers will not need access to participant data they will need the help of Genomics England to invite participants to take part in interviews and/or focus groups. Some of this research will not require access to participants through Genomics England because recruitment can be (and is already being) undertaken at GMC level or even by appeals for participants through social media. The creation of a GeCIP Domain has two advantages, however. The first is that it offers the opportunity for central facilitation of participant recruitment where this would be useful. The second is that it offers the opportunity for the national co-ordination of social science research relevant to the activities of GEL and the GMS even (and perhaps particularly) where this is not being conducted through the GEL portal centrally. That is, the GeCIP can play a national leadership role in facilitating important research relevant to GEL and the GMS.
- In a very much smaller number of cases, subject to access committee approval, researchers will require access to main programme data in the research environment for their analyses. Examples might include requests for data on the ethnicity of patients, data to help build research cohorts (to be invited for interview) around diagnoses, consent characteristics or, additional findings.

An important additional aim of the Domain will be to highlight the value of humanities and social science research and to actively encourage collaborative research partnerships with the members of other scientific and clinical domains across the GeCIP.

Expected start date	**January 2019**
Expected end date	**Open-ended**

Lead Applicant(s)	
Name	Professor Michael Parker
Post	Director of the Wellcome Centre for Ethics and Humanities and Ethox Centre
Department	Nuffield Department of Population Health
Institution	University of Oxford
Current commercial links	None

Lead Applicant(s)	
Name	Professor Anneke Lucassen
Post	Director Clinical Ethics and Law (CELS)
Department	Faculty of Medicine
Institution	Southampton University
Current commercial links	None

Administrative Support	
Name	N/A
Email	N/A
Telephone	N/A

Subdomain leads		
Name	**Subdomain**	**Institution**
Dr. Anneke Lucassen and Prof. Bobbie Farsides	Ethics in Practice	University of Southampton; University of Sussex
Dr. Ingrid Slade and Dr. Mark Sheehan	Analysis of Key Ethical Concepts	University of Oxford; Oxford University Hospitals NHS Foundation Trust
Professor Michael Parker (Acting Lead)	Patient and Participant Experience	The research undertaken in this sub-domain will take the form of a cluster of research projects based at a number of different UK Higher Education Institutions. Co-ordination will be managed by Wellcome Centre for Ethics and Humanities at University of Oxford.

Sub-domain specific sections

Subdomain proposal – domain name here (1) (total max 1500 words per subdomain)	
Title *(max 150 characters)*	**Ethics in Practice:** **Ethical issues arising for health professionals and researchers in their practice**
Importance. *Explain the need for research in this area, and the rationale for the research planned. Give sufficient details of other past and current research to show that the aims are scientifically*	

justified. Please refer to the 100,000 Genomes Project acceptable use(s) that apply to the proposal (page 6).

Aims:

The aim of this GeCIP sub-domain is to combine empirical bioethics research, conceptual and theoretical analysis, and professional and public engagement to examine the concept of *ethical preparedness* in the context of genomic medicine. We define ethical preparedness as the ability and willingness to work in morally-appropriate ways, even within emerging, rapidly-changing, and complex fields such as genomic medicine. This sub-domain will bring together scholars with established and complementary experience of researching the social and ethical implications of emerging medical technologies to: (a) engage practitioners, policy makers and patients in the field of genomic medicine with the concept of ethical preparedness, and to encourage further conceptual analysis and critique of the concept within bioethics (b) adopt a range of methodologies to capture and assess current levels of ethical preparedness (c) engage professionals in a process of co-research and co-production through a shared Genethics Forum (d) translate the findings into future genomic practice and policy (e) achieve these goals through close interaction with other sub-domains

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

This sub-domain will focus on the development of a **national ethics forum** -*100K GenEthics*- for the provision of ethics support and advice, complemented by the co-ordination of ethics support and advice across the Genomics Medicine Centres. The forum will be based on the successful existing Genethics Club (www.genethicsUK.org) and will focus on the practical ethical issues that arise in the NHS delivery of genomics, and will also consider the wider implications these issues have for research and commercial developments.

The co-ordination and delivery of **high quality ethics research**, often with a strong empirical social science component, to address (a) to what extent practitioners present and/or see themselves as ethically prepared to deliver genomic medicine? (b) whether accounts of patient experience contribute to an understanding of ethical preparedness (c) whether the concept of ethical preparedness be articulated in a way that allows it to be used to good effect in other areas of medicine?

The affordable availability of detailed readouts of a whole genome sequence (WGS) may indeed help guide diagnoses and treatments, but it might also lead to us to gathering and storing information we are unused to interpreting, sharing, or maybe even justifying. Whilst this is often represented as a temporary problem that will be solved by the development of bio-informatic algorithms and tools for interrogation of the genome, this ignores inherent complexity. Identifying a disease related genomic factor may be only one piece of a jigsaw puzzle that does not predict much, if anything, about the final picture, and whose remaining pieces cannot be found simply by cheaper and faster genomic analyses or improved technology. Health services need to be prepared to face new challenges born of the complexity, uncertainty and longevity of the clinical encounter in this field.

Subdomain proposal – domain name here (3) (total max 1500 words per subdomain)	
Title *(max 150 characters)*	**Analysis of Key Ethical Concepts**

Importance. *Explain the need for research in this area, and the rationale for the research planned. Give sufficient details of other past and current research to show that the aims are scientifically justified. Please refer to the 100,000 Genomes Project acceptable use(s) that apply to the proposal (page 6).*

This sub-domain is important for the translational aims of the 100KGP programme and future implementation of genomic medicine in the NHS. Achieving appropriate integration of genomic medicine into healthcare services will require consideration of multiple factors related to the healthcare system including, but not restricted to, balancing the needs of different groups of patients, ensuring fair access to genomic medicine for all members of the population, considering the areas of genomic medicine that are clinically effective and deciding which are a fair use of commissioning resources, setting fair priorities for genomic services across the NHS, translating these priorities into the necessary service plans for local populations and then supporting the development of these services, monitoring and continuously improving services in response to new "bench" advances and getting these results into practice, providing ongoing training and education of the workforce and ensuring high quality services by analysing risks and ensuring resolution when required.

Becoming clear about ethical concepts and principles, both generally and in specific practical contexts requires sustained ethical and conceptual analysis as well as thorough examination of the range of relevant ethical arguments. This sub-domain and the projects that fall within it take this methodology as its primary focus. Unsurprisingly, how we understand ethical concepts, arguments and their importance is also dependent on both the practices in which they are to operate as well as the experiences of those within those practices. Consequently, each of the projects within this sub-domain is also importantly oriented towards the experience of those involved in the work of the 100KGPand the GMS and will benefit from and be complementary to the work of the other ethics and social science sub-domains.

Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*

To conduct comprehensive research in to the exploration of attitudes we would work with the patients, clinicians, researchers and policy makers. This ethics sub-domain will interact and collaborate with the other sub-domains within the ethics and social science domain, in particular the 'Ethics in Practice' sub-domain, and with researchers in other domains, such as the one focusing on health economics. This sub-domain will also seek to work within a network, bringing together other researchers, policy and healthcare decision makers within the ethics and social science GeCIP as well as to increase awareness and understanding of the issues to help prepare for the integration of genomic medicine in the NHS. In addition, the ethics research conducted under this sub-domain will complement the basic science and clinical research by addressing how, in each context (oncology, infectious disease, rare disease) the genomic medicine interventions, the associated care pathway and their attendant ethical issues feed into the ethical principles applicable in the integration of genomics into the NHS.

Scope and Aims of Ethical Analysis of Key Concepts Sub-Domain
The format of each of the projects within this sub-domain, listed below, reflects these overarching aims. That is, each project begins with ethical and conceptual analysis and then proceeds to engage in various ways with practice in an effort to embed the analysis within practice and policy in a robust and relevant way.

Aims of the Ethical Analysis of Key Concepts Sub-Domain:

- To explore, through both conceptual and empirical analysis, the key ethical concepts arising through the broader work of the 100K Genome Project
- To identify, through rigorous ethical and conceptual analysis of key concepts, how areas of current NHS structures, systems and practice might need to evolve in an ethically appropriate way in the integration of genomics into medicine
- To undertake this ethical and conceptual analysis to practically inform and assist the 100K Genome Project in its aim of integrating genomics into the national healthcare system
- To work closely with other Ethics and Social Science sub-domains to ensure effective and productive research collaboration

Scope of the sub-domain

The work of the projects within the sub-domain will focus on the following three areas:

- Research ethics including consent, uncertainty, and professionalism in biomedical research, incidental findings
- Clinical Ethics including consent, incidental findings and the role of family in genomic medicine
- Public Health and Policy Ethics including resource allocation and priority setting and commercialisation in genomic medicine

Key research topics to be addressed include:

- Fundamental uncertainty, consent and research ethics
- The concept of professionalism in genomic and data-driven research
- Genomic medicine and the family
- Priority setting and resource allocation in genomics
- Commercial interests and genomic medicine
- The return of incidental findings and the nature of research ethics in genomic medicine

Subdomain proposal – domain name here (4) (total max 1500 words per subdomain)	
Title *(max 150 characters)*	**Patient and Participant Experience:** **Experiences of patients and research participants of involvement in the 100,000 Genomes Project**
Importance. *Explain the need for research in this area, and the rationale for the research planned. Give sufficient details of other past and current research to show that the aims are scientifically justified. Please refer to the 100,000 Genomes Project acceptable use(s) that apply to the proposal (page 6).* The successful introduction of genomics into clinical practice and its use at the interface between research and clinical practice depends crucially upon the availability of high quality evidence about the experiences, expectations, and concerns of patients, research participants and the wider public. This research is essential to inform the development of evidence-based approaches to good practice in the clinical uses of genomics in the NHS. It is also vital for the development and evaluation of services and research programmes capable of commanding the well-founded trust and confidence of patients and the public.	
Research plans. *Give details of the analyses and experimental approaches, study designs and techniques that will be used and timelines for your analysis. Describe the major challenges of the research and the steps required to mitigate these.*	

This sub-domain has two distinct aims. The first of these is to develop and conduct social science research to investigate and gather evidence regarding the experiences, concerns, and expectations of patients, research participants, and the public. Its second aim is to play a national leadership role in the co-ordination of research of this type currently being conducted in a piecemeal and un-coordinated way across the Genomic Medicine Service and the wider NHS.

With regard to the first of these aims, this subdomain is comprised of a cluster of research projects at different scales, each concerned with the gathering of high quality evidence about the experiences of patients and family members as participants in the 100,000 Genomes Project and in the subsequent activities of the GMS. Importantly, these are not engagement activities but research activities aimed at gathering systematic qualitative and quantitative evidence about experiences, values, and concerns of patients and participants with respect to key aspects of genomics. The issues investigated are likely to include: consent, decision-making about additional findings, feedback of results, sharing information in families, attitudes to commercial company involvement, and so on. The methodologies most likely to be used by researchers in this sub-domain are going to be qualitative, with the possibility that the findings of this research will inform subsequent quantitative studies. This is appropriate because of the focus on in-depth study of experiences, values, and concerns, and also because there is a pressing need for exploratory studies in this new and rapidly evolving area of practice. The sub-domain will also likely include surveys involving larger numbers of participants.

It is unlikely that many researchers in this sub-domain will require access to data. However, in some cases, they will need the assistance of Genomics England in inviting suitable participants to take part in interviews and/or focus groups.

A number of projects are already underway. These include:

- Two Health Education England Fellowships: Lisa Ballard (Southampton) and Celine Lewis (UCL/GOSH)
- Dr Saskia Sanderson conducting research on the experiences of 100k participants at GOSH
- Dr Felicity Boardman conducting a Wellcome Fellowship on patient experiences of disability in genomics
- Dr Gill Crawford undertaking research on the experiences of patients recruited to 100k project in Southampton
- Dr Caroline Benjamin and PPI leads at several GMCs conducting research on experience of consent
- Dr Simon Woods and Dr Pauline McCormack at PEALS (Newcastle) and colleagues across England and Wales conducting research on experiences of feedback (Seeking funding through a Wellcome Collaborative Award)

With regard to the second of the aims of this sub-domain – the co-ordination of research activities at a national level – a number of activities have already taken place which have illustrated the value of this sub-domain. These include two national meetings, organised by the Genomics England in-house ethics team, to bring together social science and ethics researchers from across the United Kingdom who are doing research on patient and participant experience of genomics. These meetings have attracted large numbers of researchers and have illustrated the range and value of research projects at different scales currently being undertaken with patients and participants across the country. This work is, however, very disparate and at a relatively small scale. A degree of national co-ordination and facilitation would be useful to avoid duplication and to foster collaborative work. Against this backdrop, one of the key initial activities of the subdomain will be to conduct a survey of all patient experience research being undertaken across the GMS, the wider NHS, and in university departments. It is likely that this will be followed up with a third national

conference/symposium to bring these research groups together with each other, with scientists, and with funders.

Domain-wide sections

Collaborations including with other GeCIPs. *Outline your major planned academic, healthcare, patient and industrial collaborations. This should include collaborations and data sharing with other GeCIPs. Please attach letters of support.*

A primary aim of the Ethics and Social Science GeCIP Domain is to add value to the scientific and clinical interpretation work being carried out across the GeCIP more broadly. When this research plan is approved one of our first actions will be to work with partners to encourage contacts between researchers in this domain and others to embed consideration of ethical and societal considerations into their programmes and to offer ethics advice and support where this is required. The Cross-Cutting GeCIP Coordinator will facilitate links between scientists and clinicians and ethics and social science researchers across the range of GeCIP domains.

Training. *Describe the planned involvement of trainees in the research and any specific training that will form part of your plan.*
In addition to their research activities, the members of the sub-domains, will actively seek out opportunities to provide training in ethics to health professionals, researchers and policy makers involved in genomics. They will also work closely with Genomics England and together with the Genomics England Ethics Advisory Committee to ensure that relevant findings and lessons are taken up at Genomics England itself. A key existing resource for genomic and genetics clinicians, lab staff, and researchers is the Genethics Forum – a national ethics forum coordinated by the two leads of this Domain. This forum will play an important role in supporting genomics researchers and clinicians to identify and resolve ethical problems and to share good practice nationally.

People and track record. *Explain why the group is well qualified to do this research, how the investigators would work together.*

The sub-domains within this Domain were selected through a national call and subsequent peer review. The successful proposals were then clustered into sub-domains in order to ensure good coverage of ethical and social issues, coherence within each sub-domain, and complementarity between them. The subdomains include most of the leading researchers on the ethical and social aspects of genomics currently working in the United Kingdom.

<u>Examples of successful funding applications</u>
A number of successful funding applications, supported by Genomics England, have already been made. These include:

- Anneke Lucassen and Bobbie Farsides: Wellcome Collaborative Award to carry out the proposed research of the Ethics in Practice sub-domain
- Felicity Boardman: Wellcome Fellowship to conduct research on experiences of genomic testing and disability
- Ingrid Slade: Wellcome Fellowship to conduct research on the ethical implications of the relationship between populations and individuals in genomics
- Pauline McCormack: Wellcome Small Grant to organise a workshop on patient experiences in genomics
- Michael Parker: Wellcome Centre Grant to Establish the Wellcome Centre for Ethics and Humanities to explore ethical issues arising in genomics and data-driven research

- Two HEE Fellowships (see above)

Clinical interpretation. *(Where relevant to your GeCIP) Describe your plans to ensure patient benefit through clinical interpretation relevant to your domain. This should specifically address variant interpretation and feedback and your interaction with the cross-cutting Validation and Feedback domain.*

The Ethics and Social Science domain aims to ensure patient benefit through informing the development of high standards of ethical practice in the clinical and research uses of genomics. The activities of this domain will help to ensure that this is empirically based and informed by careful scrutiny of ethical issues. Examples of areas of practice relevant to clinical interpretation, where this might be particularly important include:

- Consent
- Sharing information in families
- Research and clinical practice with children and young people
- The return of results and the clinical impact of practices around this
- The practical ethical issues arising for health professionals

Beneficiaries. *How will the research benefit patients and healthcare institutions including the NHS, other researchers in the field? Are there other likely beneficiaries?*

- Building evidence-based and coherent consideration of ethical and social issues into the development and conduct of genomic science and medicine
- Contributing to the development of new methods and theories in ethical and social science disciplines engaged with genomics.
- It will contribute to the growth and international profile of UK social science and humanities research

Commercial exploitation. *(Where relevant to your GeCIP) Genomics England has a very explicit intellectual property policy. We and other funders need to know if the proposed research likely to generate commercially exploitable results. Do you have commercial partners in place?*

N/A

References. *Provide key references related to the research you set out.*

Ethics and the social contract for genomics in the NHS (2017) Lucassen, A., Montgomery, J., Parker, M. in Chief Medical Officer, Generation Genomes: Annual Report of the Chief Medical Officer 2017. Chapter 16.

Data requirements
Data scope. *Describe the groups of participants on whom you require data and the form in which you plan to analyse the data (e.g. phenotype data, filtered variant lists, VCF, BAM). Where participants fall outside the disorders within your GeCIP domain, please confirm whether you have agreement from the relevant GeCIP domain. (max 200 words)* No particular clinical groups of patients apart from cross-cutting characteristics such as whether secondary findings have been returned or might be returned in future, or to compile lists of participants to interview based on age or socioeconomic factors, or a particular type of diseases or patient – clinical interaction, for instance.
Data analysis plans. *Describe the approaches you will use for analysis. (max 300 words)* Data analysis in this domain will differ markedly from genomic and other computationally complex analysis performed by most other domains. For instance, it will encompass qualitative analysis methods for interview transcripts or straightforward statistical analysis of the secondary data in the Research Environment. There are no special requirements
Key phenotype data. *Describe the key classes of phenotype data required for your proposed analyses to allow prioritisation and optimisation of collection of these. (max 200 words)* Not applicable for this domain, except to create research cohorts for social science projects in the Research Environment
Alignment and calling requirements. *Please refer to the attached file (Bioinformatics for 100,000 genomes.pptx) for the existing Genomics England analysis pipeline and indicate whether your requirements differ providing explanation. (max 300 words)* N/A
Tool requirements and import. *Describe any specific tools you require within the data centre with particular emphasis on those which are additional to those we will provide (see attached excel file List_of_Embassy_apps.xlsx of the planned standard tools). If these are new tools you must discuss these with us. (max 200 words)* None initially
Data import. *Describe the data sets you would require within the analysis environment and may therefore need to be imported or accessible within the secure data environment. (max 200 words)* None initially
Computing resource requirements. *Describe any analyses that would place high demand on computing resources and specific storage or processing implications. (max 200 words)* N/A
Omics samples
Analysis of omics samples. *Summarise any analyses that you are planning using omics samples taken as part of the Project. (max 300 words)* N/A

Data access and security	
GeCIP domain name	Ethics and Social Science
Project title *(max 150 characters)*	No projects within the sub-domain currently require access to main programme data through the research environment.

Applicable Acceptable Uses. *Tick all those relevant to the request and ensure that the justification for selecting each acceptable use is supported in the 'Importance' section (page 3).*

□ *Clinical care*
□ *Clinical trials feasibility*
□ *Deeper phenotyping*
□ *Education and training of health and public health professionals*
□ *Hypothesis driven research and development in health and social care - observational*
□ *Hypothesis driven research and development in health and social care - interventional*
□ *Interpretation and validation of the Genomics England Knowledge Base*
□ *Non hypothesis driven R&D - health*
□ *Non hypothesis driven R&D - non health*
□ *Other health use - clinical audit*
□ *Public health purposes*
□ *Tool evaluation and improvement*

Information Governance

□ The lead for each domain will be responsible for validating and assuring the identity of the researchers. The lead may be required to support assurance and audit activities by Genomics England.

Any research requiring access to the embassy will be required to complete IG Training and read and sign a declaration form. Access will only be granted once these requirements have been met.