Cambridge University Hospitals NHS Foundation Trust

100,000 Genomes Project

Participant Information Sheet

This sheet summarises the project and key points that you need to consider. It includes specific sections about each of the points on the consent form. More detailed information is given on the Genomics England website www.genomicsengland.co.uk

Please ask as many questions as you want and share this leaflet with friends and family.

If you don't want to take part in this project, you don't have to. It's up to you. You don't have to give a reason and your care will not be affected if you say no.

About the 100,000 Genomes Project

Genomics England, with the consent of participants, is creating a lasting legacy for patients, the NHS and the UK economy through the sequencing of 100,000 genomes. This is known as the 100,000 Genomes Project. The goal of the Project is to transform the application of genetics to healthcare in the National Health Service.

Your genome

Your genome is all of the genetic information in your body's instruction manual. Some of your genome is unique to you, but you do share most of it with your relatives. Your genome is made of DNA which is a series of letters which can be looked at, one-by-one, using a technique called sequencing. Recent developments in science and technology mean that it has become possible to look at the whole genome.

What can sequencing a whole genome tell us?

Learning more about the work of your genes could give vital clues about the cause of disease and help to improve treatments. When different whole genome sequences of patients with the same condition are compared, it is possible to see patterns. These patterns can be put together with health information about the patient and many other participants. Once this is done we may be able to link particular patterns with whether people become ill and how severe their illness is likely to be. Sometimes these patterns can also give clues as to the best treatments for a patient, or may reveal information that could be important to other family members.

How might this affect patient care?

Allowing researchers to look at detailed information about your rare disease in combination with your whole genome sequence can help to understand your condition and to discover new ways of improving healthcare. A possible advantage of researchers from commercial companies looking at this, as well as other researchers, is that companies can help to develop new medicines, diagnostic tests and treatments for the future more quickly than the NHS itself can. This is especially important for conditions which have few effective treatments.

Why are we doing the 100,000 Genomes Project in the NHS?

Fast, low-cost, whole genome sequencing is now affordable for the NHS. Using whole genome sequencing for the benefit of patients is called genomic medicine. Although genomic medicine is already happening in the NHS in cancer care, we want to develop the evidence that may expand its use in healthcare.

What is the 100,000 Genomes Project planning to do?

This Project will sequence 100,000 whole genomes from around 70,000 people in total by 2017. In cancer patients, we will sequence both the genome of the patient and of their tumour. In rare disease patients, we will sequence the patient's genome as well as the genomes of some of the patient's close relatives (if the relatives wish to take part in the Project).

The results will be linked with patients' medical records and stored securely. By combining this information and allowing access to this resource by authorised researchers, the project aims to:

- Bring direct benefit to some participants through a better understanding of the cause of their condition.
- Make new discoveries that will help us understand why some people get ill and others don't.
- Develop a genomic medicine service for the NHS.
- Support researchers and companies of all sizes to develop new medicines, therapies and diagnostics.

The project will initially focus on rare disease, cancer and specific infectious diseases.

What is Genomics England?

The project is run by Genomics England, which is a company owned and majority funded by the UK Department of Health.

Why have you been invited to join the 100,000 Genomes Project?

You are being invited to join the 100,000 Genomes Project because you, or a member of your family, has a rare disease or condition which may, or may not, have been diagnosed yet. We will invite, (ideally) two of your blood relatives so we can compare the genome of the affected person with two relatives' genomes. Often, but not always, this will be the person's parents. Everyone who takes part will be invited to join the Project and asked for their consent.

Key point

Some patients with rare diseases may get a genetic diagnosis for their rare disease for the first time but the majority will not. It is most likely that the benefit will be for patients in the future, as everyone who takes part will be helping to develop genomic medicine services for the NHS.

What will you be invited to do?

After the project has been explained to you and you have read and considered this information sheet, then one of the clinical team will ask you if you have any further questions about the details of the Project. You will be given as much time, as you feel is necessary, to consider your decision whether to take part or not. If you decide to join the Project (by completing the consent form in discussion with someone from your health care team), you will always be welcome to ask your clinical team further questions about the Project at any time after you have joined. Your clinical team will then assume you are happy to remain in the Project unless you let them know otherwise. There are further details in this information sheet about how you can withdraw from the Project after you have joined.

You will then be asked to:

- Initial all the boxes; date and sign the consent form if you want to join the Project.
- Donate a sample(s) of blood (up to 3 tablespoons), and possibly some saliva if needed.
- Provide details such as your date and place of birth, your ethnic group and gender, any family history of illness, any current illnesses, and current treatment in the database for this Project.
- Allow us to record all clinical details about your rare disease including your medical history, any laboratory tests or imaging that has been undertaken as part of the investigation and treatment of your condition.
- Provide your contact details (including email address and mobile phone if applicable) so that authorised staff from this Project can contact you to ask you further questions about your rare disease, health and your lifestyle, or to offer you additional opportunities to participate in research.
- Your contact details are confidential to the project team and will never be shared.
- Agree that either one of your clinical team, or authorised staff from this Project may contact you directly, to ask some further questions about your health and lifestyle. An example of this type of question might be whether or not you are a smoker.

What will happen to your samples after you have donated them to the 100,000 Genomes Project?

This section covers **points 4, 5 and 8** in the consent form

- We will use your samples to extract your DNA so we can undertake whole genome sequencing (looking at all of the genetic code). This is most likely to take place in England, but it could take place abroad.
- We will also take blood samples to allow us to understand how genes work, how your DNA may be changed over the course of your life, and to measure proteins or chemicals present in your blood. In future, we may be able to do new tests on the samples that are yet to be developed.
- Instead of your name being used to identify your samples and data, they will be labelled with

a unique code number, which means you are not directly identifiable. Once the DNA sequence has been obtained from your sample, the sequence data is sent electronically for analysis. According to the results of this analysis, you will receive information relating to your 'main condition' (the rare disease which led you to join this Project).

- You will only receive additional information that might be found in your genome sequence if you have asked us to look for this.
- Subject to permission from Genomics England, authorised researchers can then analyse the data for their approved research projects within a confidential space in Genomic England's computer systems. Researchers cannot take away or copy your individual data to work on elsewhere.
- Usually, not all your sample is used up for sequencing. All the remaining DNA and any other samples we take will be securely stored by Genomics England for further medical and scientific research in a special secure 'bank' called a bio-repository. This is located in the UK.
- Your samples could be used up soon, (in which case your doctor may ask you to give us more) or they could remain stored for many years.
- There may be certain circumstances where your DNA will not be sequenced. Should this occur the explanation will be given to you by your clinical team.

Access to my data and confidentiality

What information are we asking you to donate to the programme?

This covers **points 6 and 7** in the consent form

You are being asked to:

- Give information (data) about your health to this Project.
- Allow information about your rare disease to be sent by your medical team to the 100,000 Genomes Project, including information that you might tell them yourself.
- Allow the Project to obtain information from your past medical records that span your entire lifetime, including current and past illnesses, or stays in hospital. We are asking for your permission to obtain your medical records that are held by the NHS, GPs and other bodies like local and national disease registries (these are collections of information about patients with a particular condition).
- Allow the Project to continue to access your health records electronically into the future, so we can update the medical records that we hold on you over the rest of your life. This will include receiving annual information from your clinical team charting the course of your illness.
- Allow researchers to view (but not take away) any digital images that are collected from your health records, e.g. MRI scans, and including photographs. Your doctor will have already taken these images of you/your rare disease after asking your permission. These images when combined with other data and the sequence can assist in identifying the cause of a rare disease.
- The data we keep for the Project will be in the form of electronic copies and not your original records which will remain in the NHS.
- Only people authorised and cleared by Genomics England or by the NHS Trusts will access your data.

- Your data is important for future healthcare and research and will continue to be studied even after your death.
- Please note that under the Mental Capacity Act 2005, if, while you are a participant in this Project, you are found by your clinical team to have lost 'mental capacity' **after** you have given your consent to join this Project, your clinical team will inform Genomics England of this. Legally, your reported loss of mental capacity means that the **consent you have given to join this Project can no longer be considered valid**. Accordingly, from the time that Genomics England is informed of your loss of mental capacity, **you must be removed as a participant from this study**. This means e.g. that no further data will be collected about you, and no further blood samples will be requested from you. However, the information that has previously been collected about you (including information from your samples) **prior to your loss of capacity being notified** to Genomics England, will still remain available for access by researchers into the future, in line with your original consent.
- Your clinical team will discuss the issue of your consent and your mental capacity with you, about every five years after the date at which you joined the Project. This discussion will be a part of an appropriate routine clinical appointment. If your clinical team become aware either at that point that you have lost your mental capacity, or at an intervening time, they will report this.
- If you lose capacity, an appropriate consultee can be appointed for you in line with the Provisions of the Mental Capacity Act. The consultee must be involved in your care, interested in your welfare and willing to take on this role. They will probably be a family member, but could be another person. The consultee can advise your clinical team on what you would have wanted in terms of you taking part in research. On the basis of their advice, you could therefore be re-joined into the Project as a participant. If at any stage the consultee then advises that you should be withdrawn from being a participant in the Project, this will be done straightaway.
- Please note: It is always assumed that you **have** mental capacity, unless it is reported to Genomics England that this has been lost. If you are **not** reported as having lost mental capacity whilst you are a participant, your participation will proceed in line with the consent that you have given us.
- If you have any questions about these issues, please feel free to ask your clinical team at any time.

Key point

You are agreeing that past medical records (from birth), as well as current and future information about your condition (health data) can be collected by the 100,000 Genomes Project.
You are agreeing that this information can be studied now and after your death.

What will happen to your data after you have shared it with us?

This covers **points 8, 9 and 10** in the consent form

Key point

The 100,000 Genomes Project links your genome sequence with your medical records and information about your condition and makes it accessible to researchers and organisations which an Advisory Committee to Genomics England will approve according to criteria available on our website or on request from Genomics England.

All this information is securely held, anonymised and only accessible to approved researchers for *scientific and healthcare purposes only*. You are agreeing that other people can look at your data but in a way that protects your identity (though your own medical team will always be able to access your records in full for your care).

- You are agreeing that your healthcare information can be linked to your sequenced data and stored to be compared with many thousands of other sets of such information donated by other participants.
- Your data will be used to study the rare disease that led you to join this Project and may be used to study any other medical conditions that you may have had in the past, any current conditions or any conditions that you have in the future. It might also be used as part of research that mainly looks at medical conditions affecting other people.

Who will have access to your data?

- To get the most value for healthcare from the information you have donated, this needs to be accessible worldwide. Remember that your name and identifying details are not attached to these data.
- Genomics England will put the names of all the companies or organisations which have been approved to access data and for what purpose, on the 100,000 Genomes Project website www.genomicsengland.co.uk.
- Access to your data for marketing or insurance purposes will not be allowed.

Access for commercial researchers and organisations

This covers **point 9 and 10** in the consent form

Key point

You are agreeing that approved researchers from for profit companies can have access to this data under specific conditions and rules.

- You are agreeing to let both profit-making (commercial) companies and not- for-profit organisations, such as research charities, universities or hospitals access your data.
- You are being asked to do this because this may enable new medicines, treatments and diagnostics to be developed much more quickly.
- Profit-making companies might include drug companies, those making diagnostic tests or developing faster ways to analyse large amounts of data.
- Companies will have to pay to access the data we hold, although access may cost them less if

they make their results available to all other researchers. If any financial profits are made by Genomics England, these will go back to the NHS.

- You will not benefit financially if a product or test is successful because of your participation in the Project.

Can I access my data?

- Genomics England owns the data from this project. We protect it on your behalf and decide who gets access to it, within the terms of your consent.
- You can ask for a copy of your data, although there will be a charge for providing this. Details of how to do this are on the Genomic England website or via your clinical care team.
- You can withdraw from the Project at any time and can ask that your data is not used by researchers any more.

How will we keep your information securely and confidentially?

- Your data is in a controlled access database in the UK, whose security level meets national and international data standards.
- Your name and other personal details are held separately from the data. Your data is identified only by a code.
- Researchers accessing your data will be tracked by Genomics England to monitor for misuse.
- All researchers have to show that they are respecting the laws and ethical guidelines that apply to biomedical research.
- Although researchers can look at your data and ask questions about it, they can only take away the answers to their questions (their results). They can't copy or take away any of your individual data. Revealing your data on purpose in a way that identifies you would be a legal breach against the permitted use of samples and data from the Project, and is against good research practice. Any individual or institution who misused data in this way could face criminal charges, substantial fines and would be barred from accessing our Project again. Major research funders in the UK have said that they will withdraw funding for any researcher that had done this.

Will this affect my insurance?

- Any medical treatment you have may need to be disclosed to an insurer who wants it, however:
- Under an agreement between the Department of Health and the Association of British Insurers, the results of your whole-genome sequencing carried out in the 100,000 Genomes Project are not disclosable to insurers. This is because they are part of a healthcare and research project.
- You do not therefore have to disclose to an insurer that you are part of the 100,000 Genomes Project now or in the future or reveal the results of any tests returned from the Project.
- Companies are not allowed to look at any of the data held by Genomics England for insurance purposes.

What might we contact you about in the future?

This covers **points 11 and 12** in the consent form

Key point

You are being asked to agree to be contacted in the future by your clinical team about future research and to being contacted by Genomics England for additional information.

- We ask that you are willing to be contacted in the future through your clinical team to be invited to take part in research in the future. This might include ethically approved trials of new medicines or research about your views on aspects of the Project.
- You are only agreeing to be asked. If you don't want to take part in the research when it is suggested then you don't have to.
- Your clinical team might need further samples or specific information from you but if they want this, they will ask your permission. You don't have to say yes.
- You are being asked if Genomics England may contact you directly, no more than four times a year (and likely to be less than this) for further health information. This is because you know more about your life and experience than medical staff and sometimes we may need to double check information with you.

What will happen with the results?

This covers **point 13 and 14** in the consent form

What information will you receive about your main condition?

Your 'main condition' is how we describe the rare disease for which you were invited to join this Project.

- After your genome is sequenced, the results will be analysed and a detailed report sent to your clinical team who will discuss the results with you. Results will never be given to you directly by Genomics England.
- In time, findings will be returned within a couple of weeks as the technology and our understanding of the results develops. At first this will take longer, so you may not receive some or all of the findings until after your treatment has been completed.

Key point

You are agreeing to be given the results of whole genome sequencing.

There could be no findings that explain your rare disease. The results might not come back in time to influence your care.

- Alternatively there may be information that helps guide your treatment.

- It is also possible that there will be no information to report to you.
- If something important is found, a further blood sample may be required to confirm our findings. This is because in the early stages of the project, the NHS will be double-checking all the results in order to validate them. Your clinical team will only inform you of the result after confirmation of the finding by the NHS.
- You will not be told personally about the results of research that has included your data, although details of all the studies will be published and will be made available on the Genomics England website.

What other results might be uncovered by the 100,000 Genomes Project?

This covers **point 15** in the consent form

Key point

In addition to us looking for the cause of your rare disease that led to you being invited, you can choose whether you want us to look for a limited number of 'Additional Findings' about additional rare genetic diseases, which may be relevant to your future health. If this is something that you'd like to consider, your clinician will discuss with you the list of conditions we will look for, and answer any questions you may have.

If you ask us to look for these, we will search for certain conditions known to be rare but serious or life-threatening. If you have an increased risk of the conditions on the list, these conditions can be prevented, or treated early by the NHS so that their effects might be reduced.

What information will you receive about these additional findings?

- You are being asked to decide whether you want us to look for a specific list of genetic changes that increase the chance of these additional rare diseases. You don't have to agree to this.
- These are usually unconnected to your main rare disease condition. The chance of you having them is not high.
- The person taking your consent will show you the list of these additional rare diseases, which will be fully explained to you along with the implications of a positive test, and the support that will be available to you if you choose to ask us to look for these. This list will be updated regularly over the life of the Project.
- If you don't want to agree to let us do this, then we will not look for the additional rare diseases at all and won't send details about them to your medical team.
- Where you opt to receive additional or carrier status findings it is important you are aware that the list of conditions we will look for were selected on the basis of advice from the Genomics England Scientific Advisory Committee. However, part of the purpose of offering you these options is to help us understand and build the evidence base to decide if this use of genomic testing should be part of NHS standard clinical care.

What information might you and your partner/spouse receive about conditions that might affect future children you may have?

This covers **point 16** in the consent form:

As a couple: (This option is only offered if you and your opposite-sex partner/spouse have **both** joined this Project and if you tell us that are thinking about having children together, now or in the future.)

- If you and your clinical team feel this is relevant to you, you and your partner can decide whether you want us to look for specific variations in both of your genomes that might increase the risk that any future children that you have together may have a different rare genetic disease. You don't have to agree to this.
- This information is offered if you might be thinking about having a baby together. It may allow you to understand the risks of having a child in the future with one of these additional rare diseases. This means you can be directed to medical care or support that's appropriate to you.
- You may be able to pass these additional rare diseases on to your children, but they may not affect your own health at all. They are unlikely to be connected to your main rare disease.
- You and your partner can ask the person taking your consent to show you the list of these additional rare diseases to be tested for, which will be updated regularly over the life of the programme.
- Both of you have to agree to us looking for the additional conditions on the list, and both agree to receive the results together. If either of you don't want us to do this, we will not look for the additional rare diseases and won't send details about them to your clinical team.

As an individual (for women only):

- We can also look for additional rare diseases results that can affect your future children and are influenced by only one of you in the couple.
- Our current list includes variations that are transmitted by *mothers to their male children*. If you are a woman and you would like us to do this testing we will do it, with your approval.
- This does not require your partner/spouse consent. You can also request to have the discussion about your results privately from your partner/spouse if you wish.
- If you are a woman and do not want us to look for these results then we will not look for them.

How will we handle any other findings in your genome?

This covers **point 17** in the consent form**:**

- We may find results or information that we did not intend or expect to see in your genetic data or where we are unsure of the significance of a particular result for your health.
- Incidental findings are different to the 'Additional Findings', detailed above in this sheet, because we aren't setting out to look for them.
- Incidental findings will not be fed back to your clinician to discuss with you.
- Incidental findings also include non-medical findings (such as a participant in the Project not being genetically related to someone in this Project that they believe they are related to). These will not be fed back to clinicians to discuss with you or others.

What will happen after the initial report is sent to your clinician?

All your information will continue to be held on the Project's research database(s) and added to as new records become available. If there is new knowledge about how to interpret your results, we will re-analyse your data, so further information about your results may be available for your clinician to discuss with you over time.

What are the benefits of joining the 100,000 Genomes Project?

- You might benefit in terms of your healthcare personally but you might not benefit at all.
- Other patients may benefit from the knowledge generated by this Project.

What are the risks of joining the 100,000 Genomes Project?

- **Being identified as someone taking part in the project:**
  We will always do everything we can to stop this happening. There are penalties in place, but there is still a remote risk that this could happen.
- **Giving blood samples:** there is a small risk of bruising, inflammation or fainting but no more than with any other blood sample. Experienced staff will collect the blood.
- **Future risks:** there might also be new ways in the future to link information back to you directly, but we will keep up with these developments in order to protect your data. We believe that the likely benefits of taking part in the project for participants outweigh this remote risk.

How to withdraw from the project

Key point

You are free to withdraw from the 100,000 Genomes Project at any time in the future. You do not have to give a reason.

Information about how to do this will be on our website and available through your clinical team.

If you want to leave the Project after you have joined, you are able to withdraw by asking your clinical team for a withdrawal form, completing this form and returning it to them. You can opt for either:

1) No further contact, but continue to include my samples and information in the Project:

- You will not receive further reports on findings relevant to your health care beyond the initial report that your Clinician gives you.
- You will not be contacted by Genomics England or the 100,000 Genomes Project directly any more.
- However, you would still allow the Project to use your previously collected samples and collected information would still continue to be updated into the Project's databases from your health records as usual.

Or

2) **No further contact and no further use of my information:**

- **You will completely leave the 100,000 Genomes Project.**
- Researchers will not be allowed to access your information or samples in the Project, including your clinical team.
- We will not retrieve anything further from your health or other records.
- We will make your samples and data we hold unusable by anybody. We won't be able to retrieve samples distributed to other laboratories with whom we collaborate. (Any surplus from these samples is routinely destroyed after the third party's research is completed)
- Genomics England or the 100,000 Genomes Project will not continue to contact you directly any more.
- We will only retain a record that you were once a part of the project and withdrew.
- Research that is already underway using your information and samples (or already published) cannot be stopped or removed if you then decide to withdraw.

If you withdraw, it would help researchers to know why you did so and so you may be invited to join a project looking at the reasons people withdraw. You do not have to take part in this.

Your healthcare team will be happy to answer as many questions as you want. Please share this leaflet with friends and family if you would like to.

Thank you for considering taking part in the 100,000 Genomes Project.

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