Management of Withdrawn Participants or Ineligible Participants with no Sample

PAR-GUI-062 /Version Number 2.0

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1. Document version History

Version	Date	Description
0.1	18/07/2016	Initial structure and text
0.2	13/09/2016	Review with Laura Riley
0.3	11/10/2016	Amends by ATL
0.4		
0.5	02/12/2016	Amended post discussion with EAC
0.6	06/12/2016	Updated with comments from Jo Mason
0.7	12/12/2016	Updated with changes Amanda O Neill and clean version produced.
1.0	13/12/2016	Final draft with Tom's comments included.
1.1	09/08/2018	Updated in line with programme completion plans
1.2	14/08/2018	Updated in response to comments
1.3	25/09/2018	Clean version
1.4	25/09/2018	Addition of text on withdrawn participants
1.5	04/10/2018	Clean version
1.6	22/10/2018	Addition of text on withdrawal form
1.7	23/10/2018	Comments from Tom Fowler and link to supporting files
1.8	30/10/18	Amended 4.3 with comment from Tim Rogers
2.0	01/11/2018	Final version

2. Introduction

Registered participants must be removed from the 100,000 Genomes Project when they have chosen to withdraw their consent to participate or they are considered ineligible.

A participant is considered ineligible because either through further investigation prior to sequencing the patient's disease type does not fit the eligibility criteria, (for example in cancer programme participant tumour is found to be non-invasive or non-malignant); or it is not possible to obtain a suitable sample for the reasons outlined below.

1. Where the sample has failed during the process post submission to Genomics England and it is not possible to source a replacement sample. In these cases Genomics England should be notified that no replacement sample can be provided.
2. There is insufficient DNA extracted from a tumour or germline sample.
3. The DNA from a tumour or germline sample does not meet the quality thresholds of the processing requirements outlined in the Sample Handling Guidance.
4. The tumour sample does not meet the cellularity thresholds as defined in the Sample Handling Guidance document or there is insufficient tumour post neoadjuvant treatment.
5. It has not been possible to obtain a sample from a participant within the programme timelines.

If the participants disease type is found to be ineligible after sequencing has been completed they would remain in the programme but the offer to them may be limited.

Where unaffected relatives have submitted a sample but a proband sample is unavailable (either due to a failed sample, or the proband not wishing to enrol) and there are no other affected individuals in the family, it will be determined if the sample has been sequenced yet. If the sample(s) has not yet been sequenced, they would become ineligible and be removed from the programme.

If the samples(s) has been sequenced, no analysis on the genome (s) will be completed and main findings report completed. Their sequence (s) could still be provided to the research environment where it can be accessed by researchers and they would still be able to receive additional findings. It is recommended that GMCs discuss with these participants whether they would wish to continue to participate on this basis.

3. Ineligible patients

3.1. Management of data

3.1.1. Cancer

Where a registration file has already been submitted, the 'sample not sent' field should be completed in OpenClinica, which can be found under the Samples CRF. Where a participant has partially completed registration forms, these should be submitted to Genomics England prior to completion of the 'samples not sent' field. If there are any issues with completing the registration forms please contact the Service Desk.

For XML users, this data item should be completed, and the ReasonsSamplesNotSent XML submitted to Genomics England. This will ensure the data for the patients is managed appropriately in our systems.

To support NHS GMCs with this work we are able to provide a bulk upload tool to enable multiple samples not sent records to be updated in DAMS. This can be used for participants registered on either OpenClinica or XML but please note the records will be directly updated in Mercury so this update would not appear in OpenClinica. Guidance on how to use this tool (Bulk Upload Guidance) can be found at: https://www.genomicsengland.co.uk/information-for-gmc-staff/data-submission-guidance/

Where data has been collected but not submitted to Genomics England, the GMC should manage the data according to their local SOPs.

3.1.2. Rare Disease

There is currently no automated system in place so NHS GMCs are requested to notify us via the Service Desk with list of participants that are ineligible and their participant id. Please specify if the ineligibility is due to it not being possible to provide a sample or if they do not meet the disease inclusion/exclusion criteria. These will be marked as ineligible on the Genomics England systems and their data managed appropriately. Any partially completed registration forms in OpenClinica should be submitted prior to notifying Genomics England of the patient ineligibility.

3.2. Management of samples

All other samples held locally for ineligible patients, including the germline or any -omics, should be destroyed according to local SOPs unless an alternative appropriate consent has been sought from the participant that enables those samples to be kept.

3.3. Communication to patients

The NHS GMCs should follow local SOP's to communicate to the patient that their sample is not eligible for sequencing in the 100,000 Genomes Programme. A template letter for this is available here https://www.networks.nhs.uk/nhs-networks/gmc-network/documents/cancer-no-results-letter-draft/view

4. Management of withdrawn participants

Full participant literature including how to withdraw, is available on the Genomics England website, this lists the various options for withdrawal and provides the contact details for this process: https://www.genomicsengland.co.uk/taking-part/patient-information-sheets-and-consent-forms/

Participants should be reminded by their NHS GMC that they are welcome to discuss concerns about their participation with their clinical team at any time, or to visit the Genomics England website for information on types of withdrawal. If participants express a wish to withdraw, the clinical team should discuss with them the withdrawal options available to them and what these may mean for them.

4.1. Participants can withdraw partially or fully. In both options defined below, 'any further' means from the point that Genomics England confirms to the participant's clinician that the withdrawal form has been received. Partial withdrawal

'No further contact' means that Genomics England would no longer contact the participant via their clinical team, or directly (for example to feedback updates to clinical report/additional findings, invite to future research projects or send newsletters). Genomics England would no longer contact the participant on behalf of the Discovery Forum, or GeCIP researchers. However, the participant's information and any previously provided samples will be retained and used. In addition, Genomics England can get and use further information from health records in line with the consent given by the participant. This level of withdrawal leaves the 100,000 Genomes Project dataset intact and will allow researchers to continue to study disease with the goal of improving knowledge and health. It does not prevent the NHS GMC, however, from contacting the participant about the Project e.g. to discuss whether they would like to receive results.

The clinical team will still be sent the initial report about the participant's rare condition or cancer and they can ask the participant if they want to receive this. However, no further reports relevant to the participant's healthcare (such as additional findings or updated main results) would be returned after partial withdrawal.

It is still considered appropriate to include the whole genome sequence and clinical data in the research environment for use in any cohort analysis. It could also be used for any genome reanalysis but in both cases there would be appropriate safeguards in place and no further results identified could be communicated to the relevant NHS GMC.

All existing clinical data would continue to be held on the Data Acquisition and Management systems (DAMS). Data refreshes would still be expected from the NHS GMC for that patient and it would still be considered appropriate to access data from NHS GMCs or additional data sources and to manage any queries on the data with the NHS GMC.

It would be possible for Genomics England to request additional samples already stored at NHS GMCs, however new samples would not be requested.

4.2. Full withdrawal ("no further use")

This means the participant no longer wants be a participant in the Project. The clinical team will still be sent the initial report about the participant's rare condition or cancer and they should ask the participant if they want to receive this. However, no further reports relevant to the participant's healthcare (such as additional findings or updated main results) would be returned after full withdrawal.

Once the initial report has been returned, Genomics England will no longer contact the fully-withdrawn patient, obtain anything further from health records or other records, ask for more samples or any further information. Samples collected previously would no longer be available to researchers and the patients' data would be removed from future releases of research datasets into the Research Environment. Once the initial report has been returned to the NHS GMC, all existing sample material and data will be put beyond use.

4.3. Notification of withdrawal

To allow the clinical team and the Genomics England to action the withdrawal, the participant or parent giving consent on their behalf, or consultee (in the case of adults lacking capacity to consent of their own behalf), need to request and complete the appropriate Withdrawal of Consent Form and return it to the NHS GMC (currently 6a (for adult participants and parents) or 6b (for consultees) in the patient literature). If a withdrawal has been expressed verbally and it is not possible to get the participant to fill in the withdrawal form, the clinician must submit a valid withdrawal form on their behalf.

This form is available via the participant's clinical team at the NHS GMC and also downloadable on the Genomics England website. The participant will be asked how they would like to withdraw (or would like the participant to do so). The differences between the withdrawal options available should be explained by clinical team.

When completed, a copy of the signed withdrawal form should be given by the clinical team to:

The person who completed the form; and

The participant's clinical team – to be retained locally in the participant's medical notes.

The NHS GMCs are responsible for completing the withdrawal data process depending on which system was used for the participant's registration. If the participant was registered on OpenClinica, the NHS GMC are responsible for completing the withdrawal section on OpenClinica. If an NHS GMC recorded the participant's registration by submitting an XML file, they are responsible to record the participant's withdrawal by providing an XML submission of the consent withdrawal section of the data specification and uploading the withdrawal form to the Genomics England secure FTP server (sFTP).

For every withdrawal, the NHS GMC must upload a scanned copy of the participant's signed withdrawal form through the same method, either through OpenClinica or upload to the Genomics England secure FTP. The NHS GMC should notify the Genomics England Service Desk that a withdrawal has occurred.

If the withdrawn participant is a relative, NHS GMCs are also requested to change the family ID's on those participants' registrations to the respective PIDs prior to withdrawal of the participant so as to remove them from the proband's family ID enabling the case to continue progressing through the pipeline.

If the withdrawn participant is the proband, it is recommended that the GMC's discuss with the relatives whether they wish to remain in the programme or also be withdrawn. If the proband withdraws prior to sequencing, the whole family will still be sequenced but it may not be possible to provide a main findings report. It would still be possible for their genome to be used for research and for additional findings to be returned.

If the withdrawal form has been completed in error, or if the person who completed it changes their mind after returning the form, then the NHS GMC should contact Genomics England directly, as soon as possible, to avoid unnecessary destruction of samples and data. However, this may not be possible, depending on the timing.