NHS England

NHS TERMS AND CONDITIONS FOR THE PROVISION OF SERVICES

SCHEDULE 5 – SERVICES SPECIFICATION

ANNEX B: APPROVED LIST OF CANCERS AND THEIR ELIGIBILITY CRITERIA

Document Purpose	Contract
Document Name	Annex B – Approved List of Cancers and their Eligibility Criteria (v5.5)
Author	Sue Hill, CSO, NHS England
Target Audience	Programme Directors, Clinical Leads (Cancer) and Project Managers within NHS Genomics Medicine Centres (NHS GMCs)
Additional Circulation	Genomics England, Department of Health (100,000 Genomes Project, Office of Life Sciences)
Description	Approved list of cancers and their eligibility criteria for use by NHS Genomic Medicine Centres as part of the 100,000 Genomes Project.
Cross Reference	100,000 Genomes Project NHS Terms and Conditions for the provision of services (NHS GMC Contract)
Superseded Documents	Annex B of Schedule 5 – Service Specification of NHS Terms and Conditions for the Provision of Services – Version 5.0 dated 9 February 2017.
Action Required	NHS GMCs to only recruit patients with conditions corresponding to the eligibility criteria as set out herein

Version	**Date**	**Amendment History**
Version 1.0	25 February 2015	Initial Release
Version 2.0	22 January 2016	Updated Release
Version 3.0	29 April 2016	Updated Release
Version 4.0	26 July 2016	Updated Release
Version 5.0	9 February 2017	Updated Release
Version 5.5	21 April 2017	Interim Update

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Unless otherwise specifically excluded, all samples from invasive malignancies are eligible. Samples may be from the primary lesion, or from a metastasis.

General recruitment principles

- All participants must receive all usual clinical care.
- Tumour samples should be obtained as fresh or fresh frozen and not FFPE and pathways of care to facilitate this collection should be established. In a limited number of allowed circumstances optimised FFPE (see sample handling guidance) will be accepted (note the genomic interpretation will be lower quality).
- Access to appropriate high quality DNA from both tumour and germline samples enabling Whole Genome Sequencing is required.
- Samples must have been processed according to the requirements set out in Annexes F and H, and any other standard operating procedures issued during the Term.
- Potential participants not wanting to consent for the study or participate in all aspects of the Project should be excluded. The patient may opt out of receipt of secondary findings not relevant to their cancer diagnosis.
- Recruitment after negative results from another research project - a patient who has had Whole Genome Sequencing as part of another project should not be recruited to the 100,000 Genomes Project (unless otherwise agreed) as this will be unlikely to provide additional information.
- There is a requirement to provide Essential Sample Data and Core Data, therefore potential participants seen from another centre for specialist care, or where only Samples are received, cannot be recruited unless sufficient data will be obtainable from local centres.
- All potential participants must be residents of England, Scotland, Northern Ireland or Wales and be under the care of and be followed up by the NHS in England. Those in England and Wales must have an NHS number and those resident in Scotland or Northern Ireland their country equivalent.

Inclusion Criteria for Cancer

- Patients must have a diagnosis from a WHO/IARC cancer classification.
- Ability to collect the specified dataset within agreed timescales.

- Provision of informed consent in accordance with the Services Specification, Annex N – consent and patient recruitment and the Genomics England Protocol.
- ***Previously treated patients.*** With the exception of haematological malignancies patients are now eligible who:
    - present with a recurrence of a previously treated tumour (with chemotherapy, hormone therapy and/or radiotherapy). This may be a local or metastatic recurrence.
    - have undergone chemotherapy, hormone therapy and/or radiotherapy for their cancer, but fail to respond to this treatment and progress.
    - have received neoadjuvant therapy (treatment before intended surgical resection) for their tumour.
    - have undergone chemotherapy, hormone therapy and or radiotherapy for a previous tumour.

Collection of pre-treated tumour samples (e.g. from biopsy) and subsequent treated tumour samples in a time course series will be of particular value.

- ***Stored samples*** can be used providing that <u>all</u> of the following conditions apply:
    1. Samples are Fresh Frozen (not FFPE);
    2. Samples were taken after 1 January 2015;
    3. Patients must have the potential to benefit from inclusion in the project;
    4. Where the stored sample numbers do not exceed 10% of contracted volumes; and
    5. Where all other aspects of the contractual requirements can be met including:
        - Consent for inclusion specifically in the 100,000 Genomes Project;
        - The specified dataset can be collected; and
        - Samples have been processed in accordance with the applicable Annexes and sample handling guidance and have passed the relevant QC requirements.

Where collections of DNA / samples exist and consist of more than 20 individuals or were obtained before 1 January 2015 but meet other criteria outlined, permission on a case by case basis can be given by Genomics England and NHS England for inclusion in the main programme, subject to NHS GMCs completing a proforma, available on request from NHS England.

Approved List of Eligible Cancers

Unless otherwise specifically excluded, all samples from invasive malignancies are eligible. Samples may be from the primary lesion, or from a metastasis. Samples collected at re-occurrence will only be considered for Whole Genome Sequencing if there is a primary sample available: either stored or previously submitted. Recurrent tumours without a primary sample may be submitted, where advised in writing, and will be considered if:

1. The time scale from primary tumour to the recurrent tumour is such that a strong clinical case could be put that this is in fact a second primary.
2. There was no opportunity to store frozen tissue from the primary when it was resected.

Approved cancer conditions to date are invasive forms of the following cancer types. Any rare malignancy within these organs is eligible unless specifically excluded.

- Gynaecological cancers encompassing several anatomical descriptions/sites including fallopian, endometrial, ovarian and primary peritoneal
- Lung cancer
- Prostate cancer
- Colorectal cancer
- Breast cancer
- Sarcoma (including paediatric and adult sarcoma)
- Renal cancer
- Adult Brain Tumours
- Bladder cancer
- Melanoma
- Upper gastrointestinal (GI) tumours
- Testicular cancer
- Head and Neck Cancers
- Cancer of Unknown Primary
- Childhood Solid Tumours
- Neuroendocrine tumours
- Haematological Malignancies (see Appendix A)

Exclusion Criteria for Cancer

- **Ineligible cancer types** (plans are being developed to introduce many of these during the lifetime of the Project):
    - Cervical, vaginal and vulval carcinomas
    - Endocrine malignancies
    - Squamous and basal skin carcinoma
    - Low grade haematological malignancies (see Appendix A)
    - Malignancies from eye, placenta, heart, male genital tract other than prostate and testis
    - Benign tumours
    - Carcinoma in situ (except bladder) and borderline ovarian tumours.
- Non availability of matched tumour and germline DNA samples.
- DNA of insufficient quantity or quality obtainable for Whole Genome Sequencing.

Where a patient is found to be ineligible on the basis of these criteria after initial recruitment, the patient must be informed that they can no longer be included in the project.

Document Control

Changes to the eligible cancers will be based on nomination proposals from clinicians in the wider NHS, including entities with the NHS England Genomic Medicine Centre status, as well as those in academia, industry and in other sectors. An online nomination tool for cancers for inclusion is available on the Genomics England website at http://www.genomicsengland.co.uk/nominating-a-disease/Changes. These will be considered on the basis of evidence for both patient and scientific benefit, by the Genomics England Scientific Committee that also includes NHS England representatives and may be advised by members of the relevant GeCIP domain(s). Any recommendations by this Committee will be subject to approval by the Genomics England Board which has representation from NHS England. Changes to the approved list of cancers will be communicated to all entities with NHS Genomic Medicine Centre status within the communication process agreed by NHS England. A flexible approach to delivery is expected of NHS GMC Delivery Entities to respond to these changes in the approved list of cancers as they arise but recruitment for changes to the approved list of cancers is not compulsory.

Nominations submitted for consideration must include a data set and eligibility statement.

Appendix A - Haematological Malignancies

The following haematological malignancies are eligible:

- Newly diagnosed acute myeloid leukaemia (AML) and high-risk MDS patients who are also being recruited to the AML 18/19 trial can be co-recruited into the 100,000 Genome Programme, but clinical trial sample collections take priority.
- Chronic lymphocytic leukaemia (CLL) patients who are also being recruited to the FLAIR trial.
- Newly diagnosed Myeloma containing 80% and above of CD138+ sorted/enriched cells obtained from bone marrow for DNA extraction. Where a sample has less than 80% CD138+ cells but greater than 40%, sequencing may be considered where:

    1. The patient fulfils all the other eligibility criteria
    2. The cells were column sorted
    3. A second column sort would not be feasible with an explanation as to why it couldn't be performed.

    Patients entered into clinical trials (CARDAMON, MUK9, others) can also be co-recruited into the 100,000 Genome Programme provided that sufficient cell numbers for DNA extraction are available and the quality of the clinical trial sample is not compromised.

    Documented evidence of purity of cell selection has to be provided for each patient (for example, a digital image of an MGG stained slide of sorted cells and a manual differential count of this slide or by Flowcytometry) (n=500).
- Newly diagnosed aggressive B and T-cell Non-Hodgkin's Lymphomas including but not limited to DLBCL, Burkitt Lymphoma, Mediastinal B-cell lymphoma and High Grade lymphoma NOS (i.e. new WHO grey zone category), but only if sufficient fresh biopsy/resection material can be obtained (n=500).
- Patients with an unclassified HM malignancy and unknown diagnosis (for example, MDS/MPD overlap syndromes or uncertain diagnoses where clinical presentation does not fit with pathological diagnosis) (n=500).
- Patients with CML who are extreme responders based on RQ-PCR values after 3 months of treatment (<1% >10% BCR-ABL transcripts using International Standards). Only pre-treatment samples should be submitted and the patient has to be consented retrospectively (n=80).
- Children with ALL who have not obtained MRD levels of less than 5% at day 28 bone marrow examination. Patients recruited into clinical trials can be co-recruited, but only if the quality of the clinical trial samples is not compromised.

- Paediatric AML outside of or within the MyChild trial. For sample requirements, please refer to the adult AML guidance.

Note: It is important to recognise that conventional clinical diagnosis and clinical trial samples for these cancers take priority. Where it is possible to take sufficient material or an additional sample, this can be submitted through the existing NHS GMC pathways and processes for inclusion in the 100,000 Genomes Project.

Except where explicitly included above, the following patients are excluded:

- Patients who have previously received treatment
- Stage A CLL
- CML and MPDs showing standard or good response to treatment
- FFPE samples from lymphomas
- Stored samples