Cancer Eligibility Statement

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1 Document History and Control

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1.1 Version History

Version	Date	Description
1.0	March 2016	Cancer Eligibility Statement – initial release
2.0	January 2017	Cancer Eligibility Statement – updated release
2.1	April 2017	Cancer Eligibility Statement – updated release
2.2	August 2017	Cancer Eligibility Statement – update to haematological malignancies' appendix
3.0	14/08/2017	Updated version, ready for sign-off.
4.0	05/03/2018	Including updated haematological and thyroid eligibility

Description

Approved list of cancers and their eligibility criteria for use by NHS Genomic Medicine Centres as part of the 100,000 Genomes Project.

Target Audience: Recruiting Clinicians at GMCs and LDPs.

Action Required

NHS GMCs and LDPs to only recruit patients with conditions corresponding to the eligibility criteria as set out herein.

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2 Introduction

2.1 Purpose of this document

The aim of this document is to provide an up-to-date list of eligibility criteria for cancer types approved for recruitment within the Genomics England Cancer Programme. The changes in this version of the document have not yet been updated in the contract and this will happen in due course.

2.2 Structure and background to eligibility statements

Cancer has generic eligibility criteria applicable to all types and subtypes. Where there are exceptions to this they are covered within the list of approved Cancer Conditions.

The list of approved cancer conditions will be updated periodically as new types and subtypes are nominated and assessed.

Each cancer type listed has been informed by at least one clinician specialising in the field. Therefore, we would like to take this opportunity to thank this community for providing

their expertise and understanding of the conditions so generously. Given the rapid progress in the understanding of cancer worldwide, it is important that the eligibility statements continue to be reviewed and developed over time in light of new discoveries and changes in clinical practice. Therefore we will continue our engagement with the clinical community throughout the lifetime of the project.

2.3 Summary of changes to this document

This is version 4.0 of this document changes to be recorded subsequently.

3 Eligibility Statement

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

3.1 General Guidance on Inclusion and Exclusion

- 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 exceptional circumstances, when approval has been given 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.

- Patients may be recruited in parallel to a clinical trial provided the clinical trial sample will not be compromised and the sample will not undergo Whole Genome Sequencing. If the trial involves Whole Exome Sequencing please contact the service desk to discuss the appropriateness of also Whole Genome Sequencing the tumour.
- 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.

3.1.1 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:*** patients (including those with haematological malignancies) 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 all of the following conditions apply:

  1. Samples are Fresh Frozen (not FFPE);
  2. Samples were taken after 1st 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;
     - 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 1st 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.

3.2 Currently approved cancer conditions

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.

Multiple samples can now be accepted from a single patient. These can be from synchronous tumours; metastatic and primary samples; samples from different locations within a tumour or samples taken at different time points. Detailed guidance can be accessed in the current Sample Handling Guidance.

Small tumour size is not a contraindication to recruitment and guidance on techniques for sampling small tumours is also available in the current Sample Handling Guidance.

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
- Hepatopancreatobiliary tumours
- Testicular cancer
- Head and Neck Cancers
- Cancer of Unknown Primary

- Childhood Solid Tumours
- Neuroendocrine tumours (except benign)
- Haematological Malignancies (see Appendix A)
- Thyroid cancers (except micropapillary thyroid carcinoma with no metastases)

3.3 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 other than melanomas
    - Endocrine malignancies (except Thyroid Cancers)
    - Squamous and basal skin carcinoma
    - Haematological malignancies (see Appendix A)
    - Malignancies from, placenta, heart, male genital tract other than prostate and testis or melanoma
    - 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.

Appendix A - Haematological Malignancies

The following haematological malignancies are eligible:

- All patients with a Haematological Malignancy with >40% malignant nuclei for whom treatment is imminently planned:
    - Includes all patients with myeloma with >40% CD138+ve cells providing the cells have undergone an enrichment process (e.g. column sort)

- All patients with an Acute Leukaemia as defined by WHO Classification of haematopoietic and lymphoid tumours (2016) i.e. either >=20% blasts or with a leukaemia defining genetic abnormality

- All patients with Myelodysplastic Syndromes (MDS) with >=5% blasts

- Patients with Chronic Myeloid Leukaemia (CML) who meet the following criteria:

    - Extreme responders: i.e. those patients who, after 3 months of treatment with a tyrosine kinase inhibitor, have *BCR-ABL* transcript levels (by RQ-PCR) using International Standards of either <1% (extreme good responder) or >10% (extreme bad responder)
    - Present in accelerated or blast phase (i.e. >10% blasts in bone marrow or peripheral blood as determined by morphology)
    - Have another cytogenetic abnormality in addition to t(9;22) at diagnosis (NB this criteria excludes patients with their sole cytogenetic abnormality being a variant transcript)
    - Progress from chronic phase to accelerated or blast phase

- Patients with an unclassified or unknown diagnosis e.g. Myelodysplastic/Myeloproliferative Neoplasm (MDS/MPN)[1] overlap syndromes, 'triple negative Myeloproliferative Neoplasm (defined as no variant detected in *JAK2* exon 12 or codon 617, *CALR* exon 9 or *MPL* exon 10) or uncertain diagnoses where the clinical presentation does not fit with the pathological diagnosis

[1] The term Myeloproliferative Neoplasm succeeds Myeloproliferative Disorder (MPD)

Ineligible:

- Patients with Chronic Lymphocytic Lymphoma or another Lymphoproliferative Disorder for which no treatment is planned i.e. undergoing a watch and wait management approach

- Patients with Myelodysplastic Syndromes with <5% blasts

- Patients with stable chronic phase Chronic Myeloid Leukaemia or other Myeloproliferative Neoplasms