Cancer Research UK Special Terms and Conditions and Administrative Guidelines for Human Cancer Models Initiative Clinical Hub Grants

In addition to the *Cancer Research UK Terms and Conditions and Administrative Guidelines for Research Grants and Awards* (http://www.cancerresearchuk.org/funding-for-researchers/applying-for-funding/conditions-of-your-grant) (the "**CRUK Terms and Conditions**"), the following special terms and conditions of grant shall apply:

1. This is a performance-related award in respect of which the fixed payment referred to in this letter (the "**Fixed Sum**") will, subject to the terms set out in the Grant Award Letter, be payable to the host institution in arrears in equal quarterly instalments. The final instalment will be withheld pending receipt of the final sample report. Provided that the host institution collects, and has made available to the Wellcome Trust Sanger Institute ("**WTSI**"), Samples (as such term is defined in paragraph 3.1 below) in the numbers prescribed in the Grant Award Letter, Cancer Research UK shall pay to the host institution the Fixed Sum. In the event that numbers of Samples prescribed in the Grant Award Letter have not been collected and made available to WTSI by the date prescribed in the Grant Award Letter, Cancer Research UK shall be discharged of any obligation to pay the final instalment to the host institution or shall be entitled to require that the host institution repays to Cancer Research UK the final instalment if it has already been paid.

2. Without prejudice to paragraph 1 above, Cancer Research UK may withdraw, reconcile or require repayment of part of the funding of the Award if Sample accruals are less than those required or the host institution fails to consistently provide the necessary Samples and associated data required.

This may include (but is not limited to) circumstances in which:

2.1. no matching blood sample is provided;

2.2. insufficient tumour sample to initiate the organoid derivation process or insufficient blood sample to provide a germline whole genome sequence comparator.

2.3. the paired tumour sample and blood sample provided by the host institution are identified by WTSI not to be from the same patient;

2.4. the sample is not dispatched to the courier nominated by WTSI within the timeframe and SOP set by WTSI; or

2.5. the minimum patient sample dataset as specified in Appendix 1 is not collected and made available.

3. In addition to compliance with section 4.2 and 9 of the CRUK Terms and Conditions the host institution will be required to ensure that:

3.1. Fresh tissue samples and matching blood samples ("**Samples**") in the numbers and for the tumour type(s) specified in the Grant Award Letter (the "**Target Number**") are collected and made available to WTSI. In effecting the transfer of Samples to WTSI, no restrictions should be applied by the host institution to the use of the Samples by WTSI or others for any purposes contemplated by the Human Cancer Models Initiative (as described in the Grant Award Letter) (the "**Programme**"), in particular the generation of derived organoids and other research resources from the Samples, and the distribution of such organoids and other research resources for both research and commercial purposes to third parties worldwide. A specified amount of normal tissue will also be collected in the amounts that are pre-agreed with Cancer Research

UK. Multiple tumour samples from one patient will not be counted as separate Samples by the Programme unless otherwise agreed with Cancer Research UK. In the event that the UK pilot is falling short of its overall sample targets, Cancer Research UK may at its discretion request that the host institution makes available Samples in excess of the Target Number. Should such a request be made it will be based on prior discussion with the host institution, on the same funding principles and terms and conditions and the host institution is under no obligation to agree to the request.

3.2. all reasonable steps are taken to implement the required IT infrastructure to support the electronic transfer of test requests, Samples and clinical data. This will be over a secure file transfer protocol (sFTP) and using structure XML messaging. These data will be pseudonymised in compliance with the minimal requirements for trustworthy practice for the operations of a pseudonymisation service (as described in ISO/TS 25237:208 Health Informatics – Pseudonymisation; including documentation of physical, procedural, technical and personnel control) and in accordance with NHS Information Governance (IG) principles;

3.3. patient clinical data specified by the Programme including items from the Cancer Outcomes and Services Dataset (COSD) and such other data as reasonably requested by Cancer Research UK from time to time are available for use by third parties in accordance with paragraph 3.4 below;

3.4. the terms of patient consent and necessary regulatory and ethical approvals permit, with Cancer Research UK's and WTSI's consent, (i) the creation and storage in electronic databases of anonymised genomic and clinical data derived from the Samples (the "**Database**"), and (ii) the access to the Database by third parties worldwide both for research and commercial purposes, in each case as contemplated by the Programme;

3.5. all reasonable steps are taken to support Cancer Research UK and WTSI in developing protocols for the collection of blood, cancer and matched normal tissue samples and associated clinical data;

3.6. the handling, transfer and processing of Samples is conducted in accordance with GCP and SOPs and quality assurance standards approved from time to time by the Programme's Steering Committee and project team.

4. In addition to compliance with section 5.4, 10 and 12 of the CRUK Terms and Conditions, the host institution will:

4.1. maintain authorisations and comply with the Human Tissue Act 2004, Data Protection Act 1988 (or their equivalent in Scotland if applicable) and any other applicable legislation and local ethics committee approvals, and will work with Cancer Research UK and WTSI to ensure that the necessary regulatory and ethical approvals are in place to permit access to and use of the Samples for the purposes of the Programme in accordance with paragraph 3.1 above;

4.2. ensure that adequate and informed patient consent is carried out to collect surplus blood, tumour and in up to 10% of cases matched normal tissue, in line with the principals of the Programme;

4.3. ensure that comprehensive and customary insurance arrangements are maintained (for example through CNORIS) in relation to the collection and processing and use of tissue and blood samples which insurance must provide satisfactory protection for Cancer Research UK. The host institution is solely responsible for Sample collection, processing and use by it of

Samples and shall bear sole responsibility for, and indemnify and hold harmless, Cancer Research UK fully in relation to any liability arising from a negligent act or omission or other tort relating to the collection, processing and use of the Samples and any results of the Programme by the host institution (including the use of results of the Programme by clinical staff employed or otherwise retained by the host institution);

5. Notwithstanding section 7.1 of the CRUK Terms and Conditions, Funded Intellectual Property (as defined in the Standard Terms) shall vest in Cancer Research UK or its nominee. The host institution confirms that no third parties have any rights in or to any Funded Intellectual Property that would prevent or conflict with such vesting.

6. Cancer Research UK shall ensure that WTSI to whom the Samples are sent shall agree to comply with the provisions of the Human Tissue Act 2004 as from time to time amended.

7. WTSI shall be responsible for anonymising data and creating the Database, which will be made available to the host institution.

8. WTSI and Cancer Research UK shall be responsible for implementing the organoid and data sharing arrangements with third parties set out in paragraphs 3.1 and 3.4 above during the lifetime of the Programme and shall ensure that the organoids and data are used only in accordance with the terms of the consent.

9. Without prejudice to section 12 of the CRUK Terms and Conditions, Cancer Research UK will not provide any indemnity in relation to the infringement of third party intellectual property rights arising from performance of any part of the Programme.

10. For every sample you transport to WTSI where an organoid is successfully derived, propagated and banked, WTSI will provide you with a single cryovial of the organoid together with complete details of the media requirements including where to source the components and concentrations used. You will receive both the organoid and its transport to the clinical hub free of charge. Furthermore, WTSI will ensure you are given access to the genetic data generated for each organoid. Following the sequencing of the organoids, this data will freely move to European Genome-phenome Archive (EGA) and will be available for access by the research community as specified under Wellcome Trust data sharing policy. Direct access to sequencing data will be provided by WTSI in a timely manner upon request. This requires you to have sufficient storage and the responsibility of copying the data from the WTSI export system (currently Globus) within 2 weeks of it being exported before the data is deleted. In addition, WTSI will also provide you with a list of the somatic genomic alterations generated from the sequencing data in the format of a standard WTSI report. As you will be receiving the data shortly after it is generated and prior to final QC checks having been performed, WTSI expect you to not share the data or organoid cultures until sufficient quality checks have been conducted and this has been confirmed by WTSI.

11. As soon as is reasonably practicable CRUK and WTSI will work with the participating clinical hubs to develop a publications strategy. A principal objective of the collaboration is to encourage the publication of results. The importance of publications to the academic community and NHS is acknowledged and, accordingly, all reasonable efforts will be taken to facilitate publication of results in accordance with normal academic practice and respective institutional publication policies.

Appendix 1 – Minimum patient sample dataset

Name of Clinical Hub	Smoking Status	Procedure to obtain sample	Pathology M Category
Organisation Code	Prior Lines of Therapy	Type of Biopsy	Integrated TNM Stage Grouping
Local Patient ID	Cancer Treatment Modality	Date Sample Taken	Tumour Type
Age at Attendance	Source Sample ID	Morphology Snomed	KRAS Status
Gender Code	Origin of Sample	Pathology T Category	Date Sample Sent
Ethnic Category	Type of Sample	Pathology N Category	