MCRC Biobank Access Policy

Contents

1. Access specifics

What type of samples can be accessed?

For the solid tumours, routine samples are collected in a "six-pack" per operation event. A full six-pack consists of:

1. Frozen normal[1]
2. Frozen tumour[1]
3. Fixed normal[2]
4. Fixed tumour[2]
5. Blood[3]
6. Urine[4]

[1] Frozen samples will be issued as frozen sections (stained or unstained) or complete frozen samples
[2] Fixed samples will be issued as paraffin sections (stained or unstained)
[3] Blood samples will be available as 2ml serum and/or plasma aliquots. 3ml whole blood samples are also available.
[4] Urine will be issued as 5ml aliquots. A paired urine cells sample will be available for urology samples.

Samples of cryopreserved blood, bone marrow or leucopheresis product from patients with a range of blood disorders will also available.

Applications for fresh tissue and other sample types or normal tissue from non-cancer patients can also be collected prospectively for specific projects. Please discuss your exact requirements with the Biobank before you make an application for non-routine sample collections.

Who can access samples?

Researchers requesting samples from the MCRC Biobank will be classified in one of four groups as detailed below:

a) MCRC members contributing samples
b) MCRC members not contributing samples
c) External Academic (non-commercial)
d) Commercial

MCRC contributing members are defined as:
- Active suppliers to the MCRC Biobank
- Pathologists involved in sampling for the Biobank at collaborating Trusts
- Clinicians who have actively assisted with implementation of sample collection for that particular disease group

MCRC non-contributing members are defined as:
- Researchers in MCRC institutions (The Christie, University of Manchester, CRUK Manchester Institute)

- Researchers in collaborating Trusts who are not active suppliers to the MCRC Biobank

Where competition exists for the same set of samples, preference will be given to MCRC member groups over other requestors for applications of similar scientific merit. External applicants will also be required to make an expression of interest to the MCRC Biobank before a formal application is submitted to ensure Biobank stocks are not being depleted to an unacceptable level or that a prospective collection is practical/deliverable.

Charges

The MCRC Biobank will make a charge per sample to cover its costs. The pricing structure will be as follows:

1. Commercial – TBC
2. External Academic – Full price
3. MCRC Members – 55% discount
4. MCRC Contributing Members Tier 1 – 62.5% discount
5. MCRC Contributing Members Tier 2 – 75% discount

Please note: rare or difficult to collect specimens incur additional collection costs and will be priced accordingly.

For contributing members, the level of discount will be dependent on their contribution to the Biobank. Contributions will be based on a percentage per disease group & Trust, rather than a percentage of the total number of samples in the Biobank. This is due to natural variations in sampling for the Biobank, both at a disease group level and at a Trust level. More detailed guidance relating to Contributing Member discounts will be issued at a later date. Until then, projects will be assessed on a case by case basis.

For haematological malignancy samples (blood and bone marrow), charges will be assessed according to the percentage of the banked material from one particular donor requested (e.g. if 40 cryovials of frozen blood AML blasts are available, the cost of each cryovial will be $1/40^{th}$ of the standard MCRC Biobank sample charge).

Prospective collection studies

The MCRC Biobank can accommodate prospective and tailored collections of tissue, blood and fluids for a variety of disease types. Collections from surgical patients can generally be organised directly through the Biobank, however any projects which require targeting specific non-surgical patient cohorts will often need clinical team support and facilitation.

Before submitting an application to the Biobank for any prospective collection project, please contact the Biobank to determine:

- Whether your request can be accommodated within the current resource levels
- Whether there are any existing studies where prospective collection for your interested cohort may already be taking place

Where the Biobank have reached either resource or project capacity in any one disease group, your project will be placed on a 'waiting list' and will begin once either resource becomes available, or competing projects end.

Tissue Microarrays and Archive Samples

The Biobank will accept applications from researchers wishing to access tissue microarrays (TMAs) and/or mine samples from the archive (pathology or existing research), however these types of projects will judged on a project by project basis due to the additional resources these require. Researchers wishing to carry out these types of projects must approach the MCRC Biobank for initial discussions before applying.

All TMAs must be marked up by a qualified pathologist before the TMA build is conducted. Applicants should detail which pathologist they plan to collaborate with for their TMA build.

Please note: Accessing archive collections in pathology must be done either in collaboration with a member of the clinical team who has legitimate access to identifiable information, or using Biobank staff working in a substantive or honorary role who can facilitate the anonymisation process before samples are released to the Biobank.

Projects using archived samples will be costed on an individual basis depending on the resources invested by the MCRC Biobank. Where there is resource available external to the Biobank, this will be reflected in a reduced cost to the researcher.

Please note: The Biobank is unable to accept applications for use of archived specimens collected after 1st September 2006 without specific consent to use these samples for research purposes. Archive samples collected before this date are classed as 'existing holdings' and are exempt from Human Tissue Act consent requirements.

The cost of TMA projects will also be judged on a project by project basis, however there will be a flat rate hourly fee for the construction of the TMA costed in. The related sample acquisition cost for each TMA project will vary dependant on the number of cores per TMA and where the samples have come from (Biobank, pathology, research archive etc).

Please note: All TMA blocks constructed through the Biobank will remain in the MCRC Biobank as a resource for all Biobank applicants. Sections will be released for individual studies rather than the whole TMA block, however, where required, the TMA can be 'reserved' for that particular study until it has been completed.

Data

Accompanying clinical information required with samples should be requested on the application form. If the amount of information is overly complex or detailed, additional charges may be incurred to cover time for acquisition of data. This will be judged on a project by project basis.

2. Applications for use of samples

Submitting an Application

MCRC researchers wishing to use samples from the Biobank may first make an expression of interest to the MCRC Biobank Business Manager. This may be to find out whether the types of samples required are already in the bank and if not, how long it would take for the bank to collect these samples. This will not be in the form of a pre-application, but simply done by phone or email. Potential applicants will also find out about any charges for samples at this point.

External researchers must make a formal expression of interest. The expression of interest should detail a short summary of the research idea and types and number of samples required. From here, the MCRC Biobank will determine whether a formal application should then be made. At this point, the Biobank will confirm prices for the specific samples requested.

To submit a formal application, each researcher will need to write a full scientific proposal using the MCRC Biobank Project Application Form. Please contact the Biobank for an electronic submission form. Once the application form has been completed, it should be submitted to the MCRC Biobank via the 'SUBMIT BY EMAIL' function.

An administration fee of £100 for research applications will be charged at this time.

Applications for Quality Control & Method Development

In addition to applications to the Biobank for research projects, the Biobank will also accept applications for use of samples for QC and method development work. The application process for these types of projects will differ in several ways:

i) Applicants may request whole FFPE blocks for these types of studies (as well as sample types detailed in section 1)
ii) These projects will be fast-tracked by the Access Subgroup and will not be sent for peer review
iii) A separate application form should be completed for these studies, which the MCRC Biobank will provide

Availability of samples for QC or method development work should be checked with the Biobank prior to applying. The Biobank will aim to dedicate surplus tissue blocks from large tumours for QC and method development work, which may limit available tissue samples for QC / method development to certain disease groups. Where specific tissue types are required, this should be discussed with the Biobank before submitting an application as it may be possible for the Biobank to target specific tissue /sample types.

Samples distributed for QC or method development studies will be subject to the same pricing structure as detailed in section 1 of this Access Policy.

Ethics Approval & Consent

The MCRC Biobank has generic ethics approval which allows researchers to use samples from the MCRC Biobank as long as the research falls within the broad remit of what was written in the Biobank ethics application. The ethics currently covers a wide variety of research areas and testing. However, there is a chance that applications will be submitted for research which falls outside of these areas. If this does happen, two options will be considered:

a. The applicant will need to apply for his or her own ethics to support the proposal.
b. The MCRC Biobank will submit an amendment to allow the generic ethics approval to cover the application.

The route taken will be decided on a project by project basis by the Access Subgroup.

Please note: MCRC Biobank samples are only eligible for use in cancer research projects. Any applications for non-cancer research projects will not be accepted by the MCRC Biobank.

When patients are consented for the Biobank, they have the option to consent or not for various types of research or procedures. If, for example, a patient opts out of commercial research, or genetic analysis of their samples, they may not be used for this purpose. These checks will be carried out by Biobank staff before samples are assigned to a project.

Where the MCRC Biobank is being approached to facilitate a research project or clinical trial which already has an ethics approval, this should be clearly stated in the application and the original ethics application should be submitted as a supporting document where appropriate.

Use of human tissue in animal models

Under HTA guidelines, the use of human tissue in animal models should be specifically communicated to the patient when they give their consent for research. Currently only haematological malignancy patients donating blood and bone marrow to the Biobank are routinely consented for this purpose. For solid tumours, this facility is available on a project specific basis for prospectively consent patients.

The MCRC Biobank will also request evidence of an animal licence before projects or amendments of this type are approved.

Receipt of Applications

When the application has been submitted, the applicant will be contacted to inform them:

- That their application has been received
- Of their unique reference number, which the researcher will be required to use in any further correspondence with the MCRC Biobank regarding their study
- Whether further ethical review is required
- Whether their samples are available now or will require targeted collection

3. Reviewing Applications

Who will review applications?

Applications for use of samples will be reviewed by 3 reviewers consisting of both internal and external reviewers in the form of:

- 1 specialist reviewer for that disease group (external to the MCRC)
- 2 clinicians or basic scientists (Management Board Member/ MCRC member)

Applications will be reviewed on a rolling basis. In the first instance, applications will be submitted to the MCRC Biobank who will submit to the reviewers.

Please note: In addition to the scientific review of the project, it will also be assessed by the Biobank Access Subgroup to determine if there any additional resource / sample processing implications.

How will the review take place?

Reviewers will be expected to consider each application, based on 3 distinct areas, with an overall score out of 10 to be given to the project:

- Quality
- Importance
- Impact

The MCRC Biobank scoring system and form (based on the MRC grant application scoring system) is attached as Appendix 1. Once scores and comments have been collated from the reviewers, the information will be sent out with a copy of the application and any additional comments from the reviewers to members of the MCRC Biobank Access Subgroup as part of the Rolling Programme.

Access Subgroup

The Access Subgroup (see Appendix 2 for list of members) will consider the project reviews, as well as any project logistics and operational issues which may impact on the Biobank's ability to deliver the samples requested in the application.

The Subgroup will also consider whether adequate funding is available to complete all aspects of the study, which should be detailed in full in the relevant section of the application form. The applicant should clearly state the source of funding and how much is available for all aspects of the work proposed. If funding is dependent on a successful Biobank application, this should be clearly stated in the proposal so that conditional approval can be offered.

The Access Subgroup will be notified of applications which receive a good or high score, and are given the opportunity to raise any comments or questions before approval is granted after a period of one week. For any applications which receive a low score, final Subgroup approval will be required.

Decisions on Applications

Decisions on applications will fall into one of the following categories:

- Approved with no alterations/conditions
- Approved with conditions/minor changes required
- Approval not granted – major changes and/or resubmission required
- Approval not granted – Biobank will not consider supplying samples for this type of study

The applicant will receive a letter informing them of the decision. If the proposal has not been approved, clear reasons will be given.

If the application is approved, the applicant will receive a letter informing them:

- When they can expect to receive their samples (depending on whether samples are already in the bank or whether targeted sample collection needs to take place).
- Whether there are any conditions attached for approval
- Whether a meeting will need to take place to discuss sample specifics
- Whether the project has been placed on a waiting list due to either resource or project capacity in that particular disease group.
- An invoice for the total cost of requested samples.

Material Transfer Agreement (MTA)

Once researchers have responded to any comments raised during the review process, the MCRC Biobank can send an MTA to the applicant Principle Investigator (PI) for review and completion. The PI must return a wet ink copy of the MTA for countersignature by the MCRC Biobank Business Manager before sample collection begins.

Appeals

Appeals for rejected projects will be considered on a case by case basis by the Access Subgroup. If an agreement can be reached at this stage, it will be put before the Management Board where a decision will be made to determine whether the researcher has grounds for appeal. If it is found that the researcher has grounds appeal, the Management Board will choose a fourth reviewer to score the project.

Amendments

Samples provided by the MCRC Biobank to applicants may only be used in connection with research covered under the applicants approved application. Samples may not at any time be transferred or shared with another investigator or site which has not been detailed within the applicants approved application. To add additional methods to the application which do not alter the aims of the study, or additional collaborators or sites for analysis of samples, an amendment will need to be submitted to the MCRC Biobank for Access Subgroup review as part of the Rolling Programme.

Once the Subgroup has made a decision, the applicants will be notified in the form of a letter with a review form including any comments raised (if applicable). The applicants will be provided with an updated MTA, if required, for review and signature.

Patient-Derived Xenograft Tumours

After transplantation of primary material in passage 1, the tumours grow from 3mm3 to 1250mm3, an increase of 400x in volume and therefore cell number. A 400-fold increase in cell number indicates an average 8-9 divisions of the original cells, calculated using the following: 2^8 = 256 and 2^9 = 512. Thus, by the end of this first passage in mice, they will no longer contain the original tumour cells, which will have divided many times. In addition, there is no evidence that the stromal cells co-exist by the end of the first passage as they have been replaced by mouse stroma.

Our local position regarding HTA status is that at the end of passage 1, the material is no longer considered primary human material relevant to the act.

Project Review

All projects which have a proposed endpoint surpassing 3 years will be re-reviewed at this stage. Applicants will be informed of when the review will be undertaken and the outcome.

4. Other Issues

Rare Samples

These may fall into one of two categories:

i) Samples which are rare to the bank (may not necessarily be rare cancers)
ii) Samples from rare tumours

For rare samples, the MCRC Biobank may prefer to conduct the sample analysis in-house and to give the applicant access to data only, however, this will be judged on a case by case basis.

Publications

Researchers are expected to acknowledge the MCRC Biobank in any publications which are based on data derived from research involving samples sourced from the MCRC Biobank, by including the following in the acknowledgment section of publications: “Research samples were obtained from the Manchester Cancer Research Centre (MCRC) Biobank, UK. The role of the MCRC Biobank is to distribute samples and therefore, cannot endorse studies performed or the interpretation of results.”

Researchers will be required to send to the MCRC Biobank a copy of any scientific publication resulting from research involving samples supplied by the MCRC Biobank. The MCRC Biobank will use these publications for technical progress reports to the ethics committee.

Project feedback to the Management Board

At each Management Board meeting, a summary of projects reviewed at the Access Subgroup meetings held since the last board meeting will be tabled. Summaries will detail each project’s approval status, scores received and any important issues discussed at the Access Subgroup meeting.

APPENDIX 1

Access Subgroup Members

Name	Job Title
Mr Garry Ashton	Head of Histology
Dr Richard Booton	Honorary Clinical Senior Lecturer in Respiratory Medicine
Prof Chas Mangham	Deputy Clinical Director
Professor Andrew Renehan	Professor of Cancer Studies and Surgery/Honorary Consultant
Professor Charles Streuli	Professor of Cell Biology and Director of the Wellcome Trust Centre for Cell-Matrix Research
Dr Amaya Viros	Senior Clinical Scientist / Consultant Dermatologist
Dr Caroline Wilkinson	Chief Operating Officer

APPENDIX 2

MCRC Biobank Project Review Form

Score	Indicators
Excellent quality research	

10	Exceptional.
9	Excellent, research which is (or will be) be at the forefront internationally. Addresses very important medical or scientific questions. Likely to have a high impact on medical practice, or on the relevant scientific field.
Good quality research	
8	Good, bordering on excellent.
7	Good quality research which is internationally competitive and at the forefront of UK work. Important research which will be highly productive, and likely to have a significant impact on medical practice, if applicable.
6	Good quality research, on the border between national and international standing.
5	Good quality research which is at least nationally competitive. Addresses reasonably important questions, and will be productive. Good prospects of making some impact on medical practice, or on the relevant scientific field. Any significant concerns about the research approach can be corrected, easily.
Potentially useful study	
4	Potentially useful, bordering on good quality research.
3	Research plans which contain some good ideas or opportunities, but which are very unlikely to be productive and/or successful. Major improvements would be needed to make the proposal competitive.
Unacceptable	
2	Potentially useful in some aspects, bordering on unacceptable in others.
1	Serious scientific or ethical concerns. Should not be approved.

Project Number	
Quality *Please comment*	
Importance *Please comment*	
Impact *Please comment*	
Overall Score (Out of 10)	
Comments	

Signed Date