Standard Operating Procedure:

Skeletal Muscle Biopsies

# Purpose

This standard operating procedure (SOP) describes the procedures for the oversight and conduct of skeletal muscle biopsies (not intended for diagnostic purposes) in participants.

# Scope

This SOP is applicable to all University of Birmingham (UoB) sponsored clinical research where a skeletal muscle biopsy is taken from a participant. Where clinical research is sponsored by another institution, this procedure should be followed as far as possible, and in line with the contractual agreement between the UoB and the other sponsoring institution. This SOP also applies to clinical research, approved by a UoB research ethics committee (REC), that is required to follow the UoB Principles of Good Clinical Practice (GCP) for Clinical Research (UoB-GCP-POL-001). This SOP may be used as a guidance document in all other cases.

Where a skeletal muscle biopsy procedure is not being carried out at the UoB (e.g. at an NHS Trust site), the ‘set-up and maintenance’ and the ‘biopsy collection and patient care’ sections of this SOP should be followed as far as possible, and in line with local procedures and policies.

# Implementation plan

This SOP will be implemented in line with this document’s effective date.

# Stakeholders

Note that where a clinical trials unit (CTU) is involved, the CTU may take on responsibility for aspects of a skeletal muscle biopsy. The CTU may delegate these duties further to their trials team(s). All delegation of duties will be documented e.g. using the Clinical Trials Task Delegation Log (UoB-SPO-QCD-001).

* Chief investigator (CI): the CI may delegate activities to members of their research team, although evidence of CI involvement and approval is still expected and may not be delegated where ‘no delegation allowed’ is indicated. The SOP will state where delegation is possible. For clinical research approved by a UoB REC, the role of CI may be termed the principal investigator, or the supervisor for the postgraduate research student.
* Medical supervisor: an authorised doctor (physician) with relevant experience in performing a skeletal muscle biopsy. This may be the CI where they are a physician.
* Technician: clinical research staff member, as detailed on delegation log, who performs a skeletal muscle biopsy procedure.
* Assistant: clinical research staff member, as detailed on delegation log, who assists during a skeletal muscle biopsy procedure.

# Background and rationale

A skeletal muscle biopsy (from here on termed ‘biopsy’) is a widely used procedure in both biological research and clinical medicine. It has been routinely performed by trained researchers in a university setting for over 40 years. It is used most often in the context of the study of muscle physiology/biochemistry in human health and disease.

Typically, the procedure involves obtaining a small (50-200 mg) tissue sample through an approx. 6-8 mm incision that is made under local anaesthesia. The most commonly sampled site is the *vastus lateralis*, a large muscle of the quadriceps that weighs several kilograms in adults. Thus, the sample represents only a fraction of the mass of the tissue from which it is sampled.

The purpose of this document is to explain the procedures for performing a biopsy and the necessary oversight required. Robust procedures are required when performing a biopsy to ensure the safety and well-being of the participants involved (see UoB Principles of GCP for Clinical Research (UoB-GCP-POL-001)).

In the event of an adverse event, whether or not related to a biopsy, see the Adverse Event Reporting SOP (UoB-AES-SOP-001) for reporting requirements.

For deviation and serious breach reporting, see the Deviations and Serious Breach Reporting SOP (UoB-DSB-SOP-001).

# Procedure

## Training

1. The CI (or delegate) will ensure and evidence that relevant staff are appropriately trained and informed of their roles in the biopsy procedure before undertaking their respective tasks. See the Training SOP (UoB-TRN-SOP-001) and the Clinical Research Quality Manual (UoB-CQM-POL-001) for more details.
2. Where the technician is a physician, the CI (or delegate) will ensure and evidence that the technician is appropriately trained in the project-specific biopsy procedure.
3. Where the technician is not medically trained, the technician will be trained in the project-specific biopsy procedure. They will follow the procedures outlined in the section below marked ‘Biopsy training and medical oversight for non-physicians’.

### Biopsy training and medical oversight for non-physicians

1. The technician will document evidence that they have the appropriate theoretical and practical understanding to perform the relevant project-specific biopsy procedure. See the Biopsy Training Programme and Record (UoB-SMB-QCD-001) for an example.
* The theoretical understanding will cover:
* anatomy of the muscle (including innervations, vasculature, skin and connective tissue (fascia))
* knowledge of local anaesthetics and procedures to administer them
* knowledge of the techniques for making an incision
* minimizing risk for complications and wound care
* procedures to maintain sterility
* emergency procedures.
* The practical learning will cover:
* administration of the local anaesthetic
* making an incision
* assisting taking a biopsy
* taking a biopsy
* closing an incision.
1. As a minimum, the technician will assist in 15 biopsy procedures. The technician will then perform three biopsy procedures that must be supervised by the medical supervisor before authorising the continuation of the training via the Biopsy Training Programme and Record (UoB-SMB-QCD-001) (see Declarations section). As a minimum, a further seven biopsy procedures will be performed by the trainee under the supervision of a trained and competent technician.
2. Where the technician has evidence of previous biopsy experience at other institutions, the technician will perform a minimum of three biopsies in the presence of the medical supervisor at the UoB to assess the technician’s competency.
3. Following satisfactory completion of the training, the technician will obtain authorisation from the medical supervisor via the Biopsy Sampling Permission Form (UoB-SMB-QCD-002) to perform biopsies independently (without direct supervision). Authorisation will be valid for three years and only provided where the criteria listed below are met.
* Evidence of biopsy training.
* Evidence of up-to-date Emergency First Aid at Work training (or higher).
* Evidence of a competency assessment by the medical supervisor to perform the biopsy procedure and administer the local anaesthetic.
1. The technician will provide 6-monthly reports to the medical supervisor detailing the number of biopsies performed, the number of participants who have had a biopsy, and a declaration to confirm the absence/existence of any problems during a biopsy procedure.
2. The medical supervisor will determine and document (via the Biopsy Sampling Permission Form (UoB-SMB-QCD-002)) the minimum number of biopsies to be performed annually by the technician during the three- year authorisation period. The minimum number required will be based on the technician’s previous level of experience in performing biopsies.
3. At the end of the three-year authorisation period, the medical supervisor will review and document the requirements for a renewal of the authorisation to perform biopsies (if a renewal is required).

## Set-up and maintenance

1. The CI (or delegate) will document the appropriate facilities, cleaning and decontamination procedures required to perform the biopsy procedure to minimise the risk of infection to the participant.
* See the Biopsy Record Form (UoB-SMB-QCD-004) for a template to document cleaning and decontamination activities before and after each biopsy.
* Also see the Housekeeping Schedule (UoB-CRL-QCD-006) for a template to document housekeeping activities.
* The proposed facility for carrying out the biopsy procedure should be considered as part of the risk assessment. It is recommended that the biopsy procedure is conducted at the NIHR/Wellcome Trust Birmingham Clinical Research Facility based in the Heritage Building at Queen Elizabeth Hospital Birmingham. Where this is not possible/appropriate, it is advised to discuss the use of an alternative facility with the Research Ethics, Governance & Integrity Team (REGI).
1. The CI (or delegate) will ensure the applicable ethical and regulatory approvals are in place prior to conducting any biopsy procedures, including those for training purposes. When a trainee technician under supervision is performing a biopsy, the CI (or delegate) will ensure that appropriate approvals and explicit consent from the participant are documented for the trainee to perform the procedure.
2. The CI (or delegate) will document any risks related to the biopsy procedure (e.g. in the protocol and/or risk assessment). See also Project Oversight & Quality Management SOP (UoB-POS-SOP-001) for details on performing a project-specific risk assessment.
3. The CI (or delegate) will follow the [UoB health and safety policies and guidance for biological safety](https://bham.sharepoint.com/sites/SafetyServices/SitePages/biologicalsafety.aspx), including performing a separate risk assessment for work with biological materials.
4. The CI (or delegate) will document the procedure for performing the biopsy (e.g. in the protocol, work instructions or unit-level processes). The documented procedure will include the areas listed below.
* The individual(s) who can/will perform the biopsy procedure.
* A list of required equipment, consumables and personal protective equipment (PPE). Items that will come in direct contact with the biopsy site must be sterile. It is expected that the list of required items is determined in consultation with the medical supervisor.
* A process to confirm consent and eligibility before performing the procedure, including making the participant aware of the full biopsy procedure and its associated risks. It is recommended that the process includes re-confirming consent if there is a delay between consent being given and the day of the procedure.
* An accountability log to monitor all biopsy needles used (see Biopsy Record Form (UoB-SMB-QCD-004)).
* The daily limit of anaesthetic to be used per participant. For lidocaine (also known as lignocaine), the daily use must not exceed 2 mg per kg of body mass per day.
* Details of the observation period required before the participant is discharged following the biopsy procedure.
* The procedure for handling an emergency e.g. in the event of an allergic reaction to the anaesthetic. It is also expected that the medical supervisor will be available if required (as minimum, by telephone).
* As a minimum, there must be a member of staff on site during the biopsy procedure who has up-to-date Emergency First Aid at Work training (or higher).
* The procedure for sample processing after the collection of the biopsy sample(s). See also the Sample Management SOP (UoB-CRL-SOP-003) for the handling and processing of human tissue samples.
1. Where biopsy equipment is reusable, the CI (or delegate) will set up a process to ensure appropriate decontamination and sterilisation of the equipment. If the equipment is sent to an external company for cleaning, the CI (or delegate) will adhere to applicable regulatory requirements in relation to the transport of dangerous/contaminated goods. For example, public transport (such as buses and trains) must not be used to transport contaminated biopsy needles. See [UoB health and safety policies and guidance for hazardous substances](https://bham.sharepoint.com/sites/SafetyServices/SitePages/hazardous.aspx) for more information.
2. The CI (or delegate) will have a documented procedure for the purchase, receipt, storage and use of the local anaesthetic (typically lidocaine). This procedure will include the areas listed below.
* The purchase of anaesthetic by the medical supervisor.
* The use of an accountability log to monitor the receipt and use of stock (see Anaesthetic Stock Control Form (UoB-SMB-QCD-003) and Biopsy Record Form (UoB-SMB-QCD-004)).
* The procedure for the disposal of surplus stock.

## Consent

1. The CI (or delegate) will ensure that valid informed consent is received from the participant prior to the procedure being carried out.
* See Participant Engagement and Informed Consent (UoB-PEI-SOP-001) for further details and instructions.
* As part of the consent process, the participant will be made aware of and acknowledge their understanding of the potential risks associated with the biopsy procedure. See Biopsy Information Sheet (UoB-SMB-QCD-005) for further details and guidance.

## Biopsy collection and participant care

1. The technician will perform the procedure using appropriate PPE (including sterile surgical gloves and gown). Where required, a sterile field/surface will be created to store sterile equipment and consumables for the biopsy procedure.
2. Where applicable, the assistant will open sterile packaging without touching the contents to ensure that only the technician is in contact with the sterile equipment and consumables.
3. During the biopsy procedure, the technician will change to a new needle between drawing up and administrating a solution/drug (such as the local anaesthetic) to the participant. Needles must not be re-sheathed.
4. Once the biopsy sample has been taken, the technician will transfer the sample to the assistant for processing. In the event that an inadequate sample has been obtained, the technician will seek verbal consent from the participant to take an additional biopsy sample from the same incision and will record this when documenting details of the biopsy procedure. see Biopsy Record Form (UoB-SMB-QCD-004)).
5. Where multiple biopsies are required from separate incisions, the technician will perform the biopsy using a new (different) sterile biopsy needle.
6. The CI (or delegate) will provide the participant with both verbal and written aftercare instructions and advice as well as any supplies required. This will include contact details should any issues/questions arise and any necessary consumables (such as replacement plasters and bandages).
7. The CI (or delegate) will ensure that the UoB procedures for waste storage, collection and disposal are followed.

## Archiving

1. The CI (or delegate) will archive material relating to the biopsy processes with the study/trial master file at the end of the project. See also the Archiving SOP (UoB-ARC-SOP-001) for further information.

# List of expected outputs

* Evidence of appropriate staff training.
* For technicians, not medically trained, who are performing the biopsy, evidence of:
* biopsies being performed under appropriate supervision, or, where the technician is trained, authorisation has been obtained via the Biopsy Sampling Permission Form (UoB-SMB-QCD-002)
* 6-montly reports provided to the medical supervisor.
* Evidence of a documented process for performing a biopsy and minimising the risk to the participant.
* Evidence of a documented process for the purchase, receipt, storage and use of the local anaesthetic.
* Where appropriate, evidence of the process for the decontamination and sterilisation of equipment.
* Evidence of the UoB processes for waste storage, collection and disposal being followed.

# Related documents

* UoB-AES-SOP-001 Adverse Event Reporting
* UoB-ARC-SOP-001 Archiving
* UoB-CQM-POL-001 Clinical Research Quality Manual
* UoB-CRL-QCD-006 Housekeeping Schedule
* UoB-CRL-SOP-003 Sample Management
* UoB-DSB-SOP-001 Deviations and Serious Breach Reporting
* UoB-GCP-POL-001 UoB Principles of Good Clinical Practice (GCP) for Clinical Research
* UoB-PEI-SOP-001 Participant Engagement and Informed Consent
* UoB-POS-SOP-001 Project Oversight and Quality Management
* UoB-SMB-QCD-001 Biopsy Training Programme and Record
* UoB-SMB-QCD-002 Biopsy Sampling Permission Form
* UoB-SMB-QCD-003 Anaesthetic Stock Control Form
* UoB-SMB-QCD-004 Biopsy Record Form
* UoB-SMB-QCD-005 Biopsy Information Sheet
* UoB-SPO-QCD-001 Clinical Trials Task Delegation Log
* UoB-TRN-SOP-001 Training

Access to the full UoB QMS for clinical research is available via the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx).

# References and frameworks

* UoB health and safety policies and guidance for biological safety (UoB login required): <https://bham.sharepoint.com/sites/SafetyServices/SitePages/biologicalsafety.aspx>
* UoB health and safety policies and guidance for hazardous substances (UoB login required): <https://bham.sharepoint.com/sites/SafetyServices/SitePages/hazardous.aspx>

# Abbreviations and definitions

| Term | Description |
| --- | --- |
| CI | Chief investigator |
| CTU | Clinical trials unit |
| GCP | Good Clinical Practice |
| PPE | Personal protective equipment |
| REC | Research ethics committee |
| REGI | Research Ethics, Governance & Integrity Team |
| SOP | Standard operating procedure |
| UoB | University of Birmingham |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).