

## **TAKING URINE, SALIVA, STOOL AND/OR VENOUS BLOOD SAMPLES FROM HEALTHY ADULT VOLUNTEERS**

### **1. SCOPE**

A number of studies performed in the University involve taking biological samples (human tissue) from participants, such as urine, saliva, stool and/or venous blood. A wide variety of tests may be performed on these samples, which can be used to address a range of research questions.

This Approved Procedure is intended for use by researchers operating in an appropriate clinical facility (see below for definition) within the University of Oxford, who wish to collect samples of urine, saliva, stool and/or venous blood from study participants. The Approved Procedure covers the taking of the samples - it **does not** cover the subsequent tests performed on those samples.

Certain research involving the taking of samples that consist of, or include, cells (considered to be 'relevant material' by the Human Tissue Act), requires the approval of a National Health Service (NHS) Research Ethics Committee.

Where human tissue is held in storage for less than 7 days pending transfer to a Human Tissue Authority (HTA) licensed establishment, the storage is considered incidental to transportation and an HTA licence/ethical approval is not required, provided that none of the material is used for research before transfer. An example would be where tissue for use in research is collected across a number of sites and batched before being sent to an establishment licensed by HTA for storage for research. Where this applies, studies may be reviewed by CUREC.

Where human tissue is being held whilst it is processed with the intention to extract DNA or RNA, or other liquid/subcellular components that are not relevant material (i.e. rendering the tissue acellular), such studies may be reviewed by CUREC, provided the processing takes place within 7 days and before any non-cellular component of the sample is used for research. The cellular component must be destroyed.

CUREC can review studies where human tissue containing cells is used on the day of sampling for any research purpose and subsequently destroyed (i.e. there is no storage). All other research utilising cellular material will require NHS ethics review.

Advice on applying to the [Health Research Authority \(HRA\)](#), for review by an NHS Research Ethics Committee, is available from the University's [Clinical Trials and Research Governance](#) team.

**Before submitting a CUREC application for a study involving the testing of urine, saliva, stool and/or blood samples, please refer to [Best Practice Guidance 15](#). If it is still not clear where to apply to for ethics review, then details of the research should be sent to the MS IDREC Secretariat ([via their email address](#)) in order for them to advise whether the application is likely to be suitable for review via the CUREC system. The information provided must include information about the samples being taken, the tests carried out on the samples, storage and disposal of the samples, and the procedures that will be followed in the case of identifying any abnormal results.**

This Approved Procedure does not cover the administration of any drug (or other substance) intravenously, intramuscularly or sub-cutaneously.

This Approved Procedure is intended for use when the following criteria are met (n.b. the CUREC application must explicitly demonstrate how these criteria are met):

- The study involves healthy adults (over the age of 18 and not recruited via the NHS) who are able to provide informed consent. Where blood samples will be taken, a maximum of 50ml of peripheral venous blood will be taken from the ante-cubital fossa, lower arm or back of the hand by a member of staff trained in phlebotomy
- Where blood is taken, this is done in an appropriate clinical facility
- Where the biological samples are rendered acellular prior to use in research (unless the cellular samples are used and destroyed on the day of sampling).
- Staff involved in the collection, handling, transport or storage of biological samples have received appropriate training (training may be provided as part of professional training or specific courses within the University, see the [University's biosafety training](#)).

## 2. PHLEBOTOMY

**2.1 Persons drawing blood via venepuncture must perform the procedure as per the [World Health Organisation \(WHO\) guidelines on drawing blood](#).**

### 2.2 Appropriate Clinical Facilities for Phlebotomy

Appropriate clinical facilities contain the required levels of equipment, staff and services to safely perform phlebotomy. Specifically this includes:

#### Equipment

Tourniquet, latex/nitrile gloves, vacutainers, sterile needles including butterfly needles, cotton wool, alcohol wipes, plasters, clean equipment trays and medical tape. The facility must have an appropriately private clinical room with clean, wipeable surfaces, in which phlebotomy can be performed and which contains a comfortable chair or bed for participants with a cushion/pillow/arm brace to support participants' arms while blood is being drawn. Lastly, basic facilities for dealing with participants who faint (or feel faint) during phlebotomy should be provided—somewhere they can lie down (with their legs raised if necessary) and equipment for monitoring blood pressure.

#### Staff

Phlebotomy will be performed by a trained member of staff. There must always be one other staff member within the building (who is readily contactable) when phlebotomy is performed.

#### Services

An appropriate sharps disposal service must be in place (i.e. there should be sharps disposal bins that are regularly checked and safely disposed of). The facility must have a needle stick policy in place, which includes a clear statement about who to contact in the event of a needle stick injury. There must also be an appropriate laboratory for processing the blood samples, or an established safe system for transporting the samples to such a laboratory.

### **2.3 Cannulation**

Where several blood samples will need to be taken over a period of time, it may be preferable to insert a venous cannula. This will reduce the potential stress and discomfort associated with multiple sampling. Note that cannulation is considered a medical procedure and may only be conducted by, or under the close supervision of, a medically qualified practitioner.

The cannula is introduced into the vein by a needle (similar to blood drawing), which is subsequently removed while the small plastic cannula remains in place. The cannula is then fixed by taping it to the patient's skin or using an adhesive dressing. To maintain patency a sterile saline infusion / flush should be used. Flushing is not normally required before initial use, but would be conducted before each sample is collected, and the initial subsequent sample discarded to avoid contamination.

### **2.4 Collection of Urine, Stool and/or Saliva Samples**

Saliva samples may be either taken by a trained researcher, or the participant is sent full instructions together with a saliva collection kit. Stool and Urine samples should be taken only by the participant.

Urine, stool and/or saliva samples will be collected by the participant following explanation of the collection process by a researcher. Appropriate equipment must be provided to participants (i.e. sealable containers for stool/urine samples or saliva collection tubes for saliva samples). Samples may be taken at the research site or elsewhere (e.g. the participant's home) as required by the study. In studies involving the transport of samples (e.g. from the participant's home to the research site), it is the Principal Investigator's responsibility to ensure that this is done in line with regulations for the transport of hazardous materials ([University courses covering this topic](#) are provided).

## **3. TRAINING OF RESEARCH STAFF**

It is the responsibility of the study Principal Investigator to ensure that all researchers involved in collecting samples have been adequately trained in the procedures used to collect, handle, transport, store and analyse samples. Researchers who will take blood must have completed formal training in phlebotomy. This may have been during broader clinical training (e.g. doctors, nurses, trained phlebotomists) or, for non-clinical staff, the phlebotomy training course provided by various NHS Trusts or external agencies. As some of these courses involve training on mannequins, staff who complete them must only take blood from participants under direct clinical supervision until a fully trained clinician (i.e. doctor, nurse, phlebotomist) is satisfied that they may perform the procedure safely on their own. As participants may sometimes faint before, during or after the taking of blood, at least one member of staff (present in the building) must be trained in basic life support. Lastly, all staff performing phlebotomy must have evidence of Hepatitis B immunity following immunisation and be fully up to date with the standard vaccination schedule, including tetanus.

## **4. METHODS FOR RECRUITING PARTICIPANTS**

Methods for recruitment/sampling will depend on the study.

## **5. INFORMATION PROVIDED TO PARTICIPANTS**

Participants should be fully informed of all procedures involved in the research study. For studies involving the taking of biological samples the Participant Information Sheet should describe the

number and timing of the samples as well as a brief description of the reason for the sample(s). For blood samples, the volume to be taken must be stated, ideally in terms of mL and spoonfuls (5mL = 1 teaspoon; 15mL = 1 tablespoon). The PIS should also contain information about what will be done with the samples (i.e. whether they will be stored for any length of time, when they will be destroyed). The information sheet must include a statement to say what process would be followed, should a clinically significant abnormal result be identified in the course of the research. Lastly, for studies involving phlebotomy, the Information Sheet must contain a brief section on the possible risks, most commonly fainting, pain and bruising.

The Information Sheet is written in simple but non-patronising language. Most word-processing packages provide readability statistics for a document, and one should aim for a 12-year-old (Year 7) reading level for adults.

Please refer to, and use, the **Information Sheet associated with this Approved Procedure**.

## 6. CONSENT OF PARTICIPANTS

Written consent will be obtained from all participants using the **Consent Form associated with this Approved Procedure**, which includes explicit consent for the taking, storing and testing of the samples.

Please also see CUREC's [guidance on the informed consent process](#).

## 7. FINANCIAL AND OTHER REWARDS TO PARTICIPANTS

Participants may be reimbursed for their time and travel expenses either through payment or vouchers. Researchers should be sensitive to the ethical issues surrounding offering of excessive inducements to participate in research. However it is equally unethical to fail to reimburse participants adequately for their effort and time. Adverts will inform participants that they will be reimbursed for their time and expenses but the amount of reimbursement will not be revealed until potential participants contact the research team.

## 8. POTENTIAL RISKS TO PARTICIPANTS/RESEARCHERS/OTHERS AND WHAT WILL BE DONE TO MINIMISE THEM

### 8.1 Risks to participants

Common risks associated with phlebotomy are pain during the procedure and bruising (with associated pain afterwards). These risks will be minimised by ensuring that all staff are fully trained in phlebotomy. Bruising after the event will also be reduced by promptly applying pressure on the puncture site after the needle is withdrawn. All participants will be fully informed about these risks in the Participant Information Sheet.

The worry associated with taking blood may cause some participants to feel unwell or faint before, during or after the procedure. The risk associated with this will be reduced by having an adequately equipped facility for performing the procedure (see above) and having a staff member trained in basic life support.

Although phlebotomy is a very safe procedure, it does create a puncture wound on the skin which may very rarely lead to infection around the puncture site. The risk of infection will be higher where

participants have been cannulated. Other complications of cannulation include phlebitis (inflammation of the vein), extravasation (leakage into tissue surrounding cannulation site), air embolism (blockage caused by air/gas bubble in the vein), and haemorrhage (bleeding). Risks of any of these occurring will be minimised by ensuring that all staff are fully trained to undertake the procedures, and that a strict hygiene regime is followed. Where appropriate, participants who are at increased risk of infection will not be recruited. In the event that a participant reports symptoms of an infection (local redness, swelling, pain or discharge of pus) or other complication, they should be referred to their GP or to A&E urgently.

There are no risks to participants in providing saliva samples. For urine and stool samples, the main considerations are to ensure proper hygiene when samples are taken and to sample in a way that minimises embarrassment to participants.

## **8.2 Risk to Researchers/Other Staff**

The risk of exposure to infection is increased in all those involved in the collection, transport, storage or processing of any biological material. This risk will be minimised by ensuring all staff involved in these procedures are adequately trained and that the appropriate equipment and facilities for the safe handling of samples is provided. Projects involving biological samples should undergo a Departmental Risk Assessment.

- Where appropriate, participants should be screened to exclude those who suffer from communicable diseases
- Researchers who handle biological samples should clean hands with disinfectant soap or wipes before and after handling the samples, and wear latex or nitrile gloves at all times when handling samples (not vinyl gloves, as they do not protect against viruses). They should avoid use of sharps
- The cooler will be labelled as containing biological samples
- Samples should be handled in a microbiological safety cabinet, and the working area should be cleaned with 1% Virkon after use
- Storage and waste disposal procedures should be specified on a Risk Assessment form and comply with Departmental Policy.

Taking blood carries a risk of needle stick injury to the phlebotomist, which in turn carries a risk of exposure to blood borne infections. This risk will be minimised by a) ensuring staff are adequately trained in phlebotomy, b) ensuring staff have been vaccinated against, and show immunity to Hepatitis B and c) having a local policy for needle stick injury which describes the process of being assessed for, and receiving, post exposure prophylaxis.

## **8.3 Organisational Risk**

Researchers should be aware that the HTA requires 'relevant material' for research to be held under the governance of either NHS ethical approval or an HTA licence. Use and/or storage of cellular material outside of the terms of the Human Tissue Act will place the University in contravention of the Act. Please refer to CUREC Best Practice Guidance 15 (The use of human tissue samples from healthy volunteers: When and where to apply for ethical review) for full details.

All applicants must specify in their application the full procedures in place for use, storage and destruction of cellular material.

## 9. MONITORING AND REPORTING OF ADVERSE OR UNFORSEEN EVENTS

Adverse or unforeseen events will be reported to the departmental safety officer in the first instance and may be followed up by the University Safety officer if deemed necessary. The Research Ethics Committee will also be notified of such events.

## 10. USE OF STUDY DATA

Study results may be written up for publication in peer-reviewed scientific journals, presented at scientific conferences (in abstract or presentation formats), submitted as part of course degrees and may form part of grant applications. In all cases, results will be fully anonymised and not contain any data that could be linked to the volunteers. Study data may be entered into anonymised data repositories.

## 11. DUTY OF CARE ISSUES / CONFIDENTIALITY

Duty of care and confidentiality issues arise largely due to the results of tests on the samples, rather than taking of the samples per se. This approved procedure does not cover issues concerned with the testing of the samples, although it is expected that studies will have in place a system by which the results of the tests performed are reviewed and, where necessary, further investigations or referrals are made. The confidentiality of the results are also expected to be maintained.

## 12. DATA PROTECTION ISSUES

Data protection issues arise from the tests performed rather than sampling procedures. The CUREC guidance on data protection should be followed.

## 13. FURTHER INFORMATION

[WHO guidelines on drawing blood](#)

[CUREC Best Practice Guidance 15](#) – “The use of human tissue samples from healthy volunteers: When and where to apply for ethical review”

## 14. CHANGE HISTORY

Version No.	Significant Changes	Previous Version No.
1.0	Incorporates reference to the University Safeguarding Code of Practice and related requirements. Retitled ‘Approved Procedure’ (previously ‘Protocol’). Approved by CUREC, 19 November 2015	N/A
2.0	Expanded to include urine and saliva samples in addition to venous blood	1.0
2.1	Section 1 – minor changes to clarify HTA requirements	2.0
2.2	Updated hyperlinks for new CUREC website	2.1

Version No.	Significant Changes	Previous Version No.
3.0	Scope expanded to include stool samples Incorporation of text from the retired Best Practice Guidance 12	2.2
4.0	Addition of the procedure for venous cannulation Removal of example statements for the PIS and Consent form, referring instead to the templates for these documents Update of sections 6 and 9 to replace reference to guidelines with specific text General administrative amendments	3.0
4.1	Updated to improve accessibility	4.1

## APPENDIX A: HOW TO COLLECT A URINE SAMPLE

The researcher will give you a container and explain to you how to collect the urine sample.

You can collect a urine sample at any time of day. Urine is more concentrated the first time you urinate in the morning, so if you collect this sample it may give better test results. However, this isn't usually necessary unless the researcher tells you to.

### To collect a clean urine sample:

- wash your hands
- males should wash their penis
- females should wash their genitals, including between the labia (lips around the entrance to the vagina)
- start to urinate but don't collect the first part of urine that comes out
- collect a sample of urine 'mid-stream' (see below) in a sterile screw-top container
- screw the lid of the container shut
- label the container with your name, date of birth and the date
- wash your hands thoroughly

If the researcher gives you any other instructions, you should also follow these.

### What is a mid-stream urine sample?

A mid-stream urine sample means that you don't collect the first part of urine that comes out or the last part. This reduces the risk of the sample being contaminated with bacteria from your hands or the skin around the urethra (tube that carries urine out of the body).

### Storing a urine sample until you hand it in

If you can't hand your urine sample in within an hour, you should keep it in the fridge at around 4C (39F). Put the container of urine in a sealed plastic bag first. If the urine sample isn't kept in a fridge, the bacteria in it can multiply. This may affect the test results.

Ideally, your urine sample needs to be handed in and sent for testing within four hours. However, the researcher may still be able to use it after this time if it's been kept refrigerated.

If you can't hand your urine sample in immediately, find out how long it can be kept in the fridge. The researcher who requested the test will be able to tell you.



## **APPENDIX B: HOW TO PROVIDE A STOOL SAMPLE (POSTAL PARTICIPANTS)**

Kit contents: cardboard kidney dish, nitrile gloves, specimen tube, Royal Mail SafeBox.

You will also need: a plastic carrier bag for disposal.

*Please provide a sample from the first bowel movement of the day.*

*Please avoid contaminating your stool sample with urine: urinate before collecting the stool sample.*

- 1) Place the cardboard dish in the toilet bowl (or in your child's potty). Use the toilet normally, so your stool falls into the dish.
- 2) Put on the gloves and remove the dish from the toilet bowl. Use the small spoon attachment on the lid of the specimen tube to remove a small sample from the middle of the stool. A heaped spoonful of stool is sufficient. Place the stool in the specimen tube and close the lid tightly.
- 3) Flush the remaining stool down the toilet. Place the dish and the gloves in a plastic carrier bag, tie it securely and dispose of the bag with your normal household waste.
- 4) Following the instructions on the SafeBox, wrap the sheet of absorbent material around the specimen tube and seal the wrapped tube in the plastic zip-lock bag.
- 5) Wash your hands thoroughly with warm water and soap; pat dry.
- 6) Put the zip-lock bag into the SafeBox. Fold your completed questionnaire and signed consent form and put them into the SafeBox, then follow the instructions to seal the package. Post the SafeBox in any post box (you do not need to add any stamps). If you will not be able to post the SafeBox within two hours of taking the sample, please refrigerate it until you can post it. If you do not want to put the sample in your refrigerator, fill an unwanted cardboard or plastic tub with ice cubes, put the sample inside and store in a cool place.

## APPENDIX C: HOW TO PROVIDE A STOOL SAMPLE (COLLECTION PARTICIPANTS)

Kit contents: cardboard kidney dish, nitrile gloves, specimen tube, 2 zip-lock bags, cardboard container with lid.

You will also need: a plastic carrier bag for disposal.

*Please provide a sample from the first bowel movement of the day.*

*Please avoid contaminating your stool sample with urine: urinate before collecting the stool sample.*

- 1) Place the cardboard dish in the toilet bowl (or in your child's potty). Use the toilet normally, so your stool falls into the dish.
- 2) Put on the gloves and remove the dish from the toilet bowl. Use the small spoon attachment on the lid of the specimen tube to remove a small sample from the middle of the stool. A heaped spoonful of stool is sufficient. Place the stool in the specimen tube and close the lid tightly.
- 3) Flush the remaining stool down the toilet. Place the dish and the gloves in a plastic carrier bag, tie it securely and dispose of the bag with your normal household waste.
- 4) Place the specimen tube in a zip-lock bag and seal. Place the sealed bag inside the second zip-lock bag and seal the outer bag.
- 5) Wash your hands thoroughly with warm water and soap; pat dry.
- 6) Place the specimen in the cardboard container and put on the lid. Refrigerate the container with the stool sample until it can be returned to the researcher. If you do not want to put the sample in your refrigerator, fill an unwanted cardboard or plastic tub with ice cubes, put the sample inside and store in a cool place.