

7. SPECIAL PROGRAMME OF RESEARCH, DEVELOPMENT AND RESEARCH TRAINING IN HUMAN REPRODUCTION

GUIDELINE FOR OBTAINING INFORMED CONSENT FOR THE PROCUREMENT AND USE OF HUMAN TISSUES, CELLS AND FLUIDS IN RESEARCH

INTRODUCTION

Clinical research frequently involves, and in many cases depends on, the use of human tissues, cells and fluids, including sperm, eggs, blood, urine and saliva. The donors of such specimens are, as a rule, volunteers who participate in the research of their own free will and have given prior informed consent in accordance with established local, national or other regulations and practices. The nature and extent of the information provided to such volunteers, and on which their consent is subsequently based, is becoming increasingly important and complex in the light of recent medical and technical developments. In particular, recent advances in the fields of diagnostics and genomics have highlighted the need for donors to be given the opportunity to indicate whether or not they want the samples they are donating for a particular research purpose to be stored for use in future research and, if so, whether they want to place any limitations on the storage time or restrictions on the use to which their samples can be put in such future research.

This Guideline has been drawn up to assist researchers in dealing with the ethical issues relating to how clinical research materials are obtained, used and eventually disposed of, and the corresponding informed consent requirements. While this guideline is intended for the future collection of samples, many of the ethical considerations in this guideline are relevant also to previously collected human biological materials stored in repositories.

N.B. As with any guideline, this document is intended to set out general guiding principles on the understanding that these need to be interpreted and implemented in the context of local laws and customs. Such laws and customs may differ considerably from one location to another and especially in the context of the subject matter of this particular guideline. For example, major cultural differences exist with regard to, and therefore in obtaining samples from, deceased people and the placenta.

FACTORS GOVERNING OBTAINING SAMPLES FOR RESEARCH

When samples are to be obtained for research in the context of a planned diagnostic, prophylactic or therapeutic procedure, the patient/subject should be told that refusal to consent to provide specimens for research will not prejudice their medical or surgical care.

If the use of some of the sample for research may diminish the quality of the laboratory examination to be carried out for diagnostic purposes and this might affect subsequent treatment, this should be fully explained to the subject. (For example: research using small pieces of a prostate gland that has been removed during a prostate operation for supposed benign disease, may reduce the chance of diagnosis of an early prostate cancer because the pathologist has been deprived of some of the tissue to examine).

INFORMATION TO BE PROVIDED IN SEEKING CONSENT TO OBTAIN RESEARCH SAMPLES

As well as the usual project-specific information that will be provided to any research subject as part of the standard informed consent process (see Part 1, 4.1 of this document), the following additional information also needs to be provided in order that the potential research subject can make a fully-informed decision about whether or not to agree to her/his samples being taken and used in the proposed research:

- the nature and amount of the samples to be taken;
- the procedures that will be followed to obtain the samples for research and whether these are routine, modified routine, novel or experimental procedures;
- the risks and discomforts associated with obtaining the samples for research and whether any increased risk is presented if the procedure for obtaining the samples is a modified routine, novel or an experimental procedure;
- the nature, extent and duration of any treatment to be provided in the event of complications or injury resulting from the procedure to obtain the research sample, and who will pay for this treatment;
- the use to which the samples will be put in the research;
- where the samples and any clinical information will be kept and details of any relevant security arrangements;
- who will have access to the samples;
- how long the research samples will be kept;
- the arrangements for disposal of the samples at the end of the research project.

Furthermore, the following supplementary information should also be given, where relevant.

- Whether the results of the research will be relayed back to the research subject and in what form (pooled and/or individualized). The foreseeable consequences to the research subjects of having this information need to be explained and they should be allowed to choose not to know.
- If there are potential adverse consequences of disclosure of the results of the research, information should be given about arrangements for counselling
- Whether the research could reveal non-paternity or non-maternity.
- Whether the research may identify past or current infectious disease.

- Whether the research will generate genetic or molecular information that may predict characteristics or future disease patterns in the research subject or his or her family.
- Whether, if confidentiality is not respected and the results of the research become known, employment prospects and health insurability of the research subject may be effected.
- If the research involves gametes or tissue containing gametes (e.g. testicular or ovarian tissue), whether these gametes will be used to achieve fertilisation and produce embryos. **(If so, refer to separate guidelines on embryo and germ line research – in preparation).**
- Whether the research may lead to profit. If there is a possibility of commercial value then research subjects should be told whether or not they would receive any money or other intellectual property benefit that may result from commercial applications of the research.
- Who is funding the research. For example, whether a public institution or a private corporation, or a collaboration between the two.
- Whether the sponsor of the research is paying the researcher for each subject recruited to the study and/or for each sample obtained and, if so, the amount of such payments that will be received by the researchers.

All of the above information and the procedures to be used for obtaining consent for the collection of human materials should be included in the corresponding research protocols submitted for scientific and ethical review.

DIFFERENT TYPES OF CONSENT FOR THE USE OF SAMPLES IN RESEARCH

There is a potentially great public health benefit from research using samples from banks of human material. When obtaining consent for the collection of samples for use in a specific research project, researchers should request consent for use of the samples also in future studies. However, individuals must be free to consent for the use of their samples in the immediate specified research only, or for the use of these samples in the immediate specified research and also in future research, either of a specified or unspecified nature, as indicated below.

Fully restricted consent

In this case, the donor restricts the use of the samples to the immediate research only and does not consent to its use in any future research.

Partially restricted consent

In this case, the research subject consents to the use of the samples in the immediate research and in future research of a specified type(s) and up to a specified time in the future.

Unrestricted consent

In this case, the research subject consents to the use of the samples in the immediate research and in future research of any kind and at any time in the future.

In all of the above three situations, the consent document should specify the arrangements for final disposal of the samples, indicating when, how and by whom this will be carried out.

ANONYMITY AND CONFIDENTIALITY OF RESEARCH SUBJECTS

The identifying link between the research subject and the sample or research result may be kept or removed. Because all samples are originally linked to personal clinical information, researchers should ensure appropriate measures are in place to provide appropriate protection of medical confidentiality and privacy.

All research subjects should be given information about whether the research results can be linked to them and about the measures taken to ensure protection of medical confidentiality.

Samples may be unidentified, coded (sometimes termed linked or identifiable) or identified.

Unidentified

The identity is removed so that nobody knows from whom the sample came, and there is no possibility of tracing the donor. Removal of identity may be at the time of sample collection (samples collected in this way are known as anonymous samples) or a researcher may remove the identity or unlink the code from samples after conclusion of the research for which they were obtained (samples handled in this way are known as anonymised samples). Research subjects providing samples under these conditions should be informed that, as it will not be possible to identify their samples, it will not be possible to provide them with any personal results from the study.

Coded

The sample is labelled with a code known only to certain researchers, rather than with personal identifying information. Coding of samples may be done by the person collecting the samples, which are then given to the researcher; or the researcher may arrange with a third party to code samples. It is not possible for the researcher using the sample to link the biological information from the sample with the person from whom the samples was obtained without breaking the code. Research subjects should be given information about who has access to the code and the circumstances in which the code will be broken.

Identified

The sample is labelled with the name of the donor or other personal identifying information. Any researcher using these samples would be able to link the biological information from the sample directly to the individual from whom the sample was obtained. Research subjects should be given information about who will have access to

the samples and how personal information will be made secure against invasions of privacy and breaches of medical confidentiality.

SPECIAL CONSENT SITUATIONS

Samples from minors

Samples may be obtained from minors before they are of an age to give consent if similar samples serving the same purpose in the proposed research cannot be obtained from adults. Parents may reasonably give consent on behalf of a minor child where the sample is being collected for research that may prove to have therapeutic benefit to the minor or to other children suffering from the same medical conditions.

The parents should be given full information about how the sample will be obtained and any risks to the child. Most parents will wish to know about all risks, including remote risks, and the “reasonable person” standard should apply when giving information, namely: “*What any reasonable parent would wish to know*”.

Even where consent is not legally required from the child, researchers should obtain the child’s **assent**.

Where samples have been obtained from minors and are kept in store and where identity is retained (whether coded or not), arrangements should be made to obtain consent from the minor later, when he/she has reached adulthood, for continued storage or any proposed further research. The research protocol and consent document should specify the action to be taken in later years should it not be possible to contact the person from whom the sample was obtained.

The situation may arise where testicular or ovarian tissue is obtained from a minor e.g. before cancer chemotherapy. Gametes obtained from a minor should not be used for research without consent of the minor when he or she has reached adulthood.

Samples from mentally incompetent people

The same requirements and safeguards should be used in connection with obtaining samples from mentally incompetent individuals as are proposed in connection with minors (see preceding section). In essence, samples should only be taken from mentally incompetent people if similar samples cannot be obtained from competent research subjects. If practical, assent should be obtained from the incompetent research subject.

Samples of foetal tissue

The “reasonable person” standard cannot be presumed to apply in connection with the use of embryonic or fetal tissue for research purposes because not all reasonable people agree about the ethical status of the embryo and fetus. Therefore, a woman’s explicit consent is required for the use in research of such tissue following a spontaneous or induced termination of pregnancy.

In the case of induced termination of pregnancy, it is ethically preferable to have separate consent forms for the termination and for the use of the resulting materials in research, to ensure that the woman understands the distinction between the abortion and

the research and makes a free choice regarding each procedure. Researchers may use a generic consent form for embryonic and for fetal tissue research; it is not necessary to provide details of the research protocol on the consent form, unless it is the intention to use the tissue for homologous or heterologous transplantation.

Monetary payment or other inducement for donating embryonic or fetal tissue for research is expressly prohibited.

The placenta and other extra-embryonic tissues and fluids are generally regarded as non-fetal materials, and the “reasonable person” standard would apply to the use of these materials in research if they were obtained following normal term delivery. However, the same provisions would apply to their use in research, as would apply to fetal samples, if these materials are obtained as a result of induced termination of pregnancy.

Samples from deceased people

In the context of reproductive research, samples should normally be obtained from living adults who are able to give informed consent. Researchers should only consider using tissue from dead people when it is not possible to obtain such samples from a living donor. In these circumstances, consent should be obtained from the relatives after they have been given all relevant information that would normally be given to a living research donor.

Information should be given to the next of kin about how the sample will be obtained and whether this will mutilate the body. If a post mortem is in any case being performed then there may be no additional mutilation but in other cases information about the position, nature and extent of any incision should be given to the next of kin.

PROVISIONAL CONSENT

There are situations when it may be appropriate to obtain provisional consent at the time the tissue is taken but then to keep the research sample for some weeks or months and then to reconfirm the consent later at a time when it is intended to use the sample. This may be appropriate for samples taken during labour or for foetal tissue or samples taken from deceased people. The intention of provisional consent is to allow time for the research subject (or relatives) to reach a final decision on consenting to the use of the samples after the stress of the operation (or the immediate grief) has passed.

PREVIOUSLY OBTAINED SAMPLES

In the case of samples obtained previously without any future use provisions, researchers should try to obtain informed consent from the original donors or their proxies for the use of these materials in research studies for which they were not originally obtained. Where this is not practicable, and the research is expected to produce important public health benefits, the researcher should request the research ethics committee to waive the informed consent requirement and, at the same time, to advise on the action to be taken in contacting the donors of the samples, or their proxies, depending on the nature of the research, the significance of the results and the consequences of disclosure or non-disclosure of this information.

Appendix A

SUMMARY OF INFORMATION ABOUT RESEARCH SAMPLES THAT SHOULD BE GIVEN TO RESEARCH SUBJECTS

What the sample is and how the sample will be obtained

Degree of invasiveness.

In case of invasive procedures, any additional risks.

Arrangements for treating complications that may arise during or after invasive procedure to collect specimens.

Consequences of any variation in normal histopathological examination caused by specimen collection.

In the case of vaginal examination or other intimate examination, how privacy will be protected.

What consent is being asked

Consent for the specific research project only (fully restricted).

Partially restricted consent.

Unrestricted consent to use sample for any type or research.

Whether identity will be retained or not

Unidentified (anonymous or anonymised).

Coded (linked or identifiable).

Identified.

How will confidentiality be ensured

How confidentiality and privacy of personal information will be protected.

Where samples and any clinical information will be kept.

Who will have access to the samples and the research results.

Whether the results of the research will be relayed back to the research subject.

For how long samples will be kept.

The final disposition of the samples and information.

In addition it may be appropriate to give information about

Arrangements for disposal of the samples at the end of the research project.

If the proposed studies will involve genetic research.

The possibility of revealing non-paternity.

Detection of infectious disease.

Whether the results may affect insurability.

Whether the research involves “fertilisation”.

Whether the research involves alteration to germ lines or embryos.

That the research subject will not receive any money from commercial applications of the research.

Who is funding the research.

Whether the researcher will receive per subject payments.

What treatment will be provided in the case of research-related injury in obtaining the sample, and whether monetary compensation will be available for any such injuries.

Appendix B

EXAMPLE CONSENT DOCUMENT FOR AN INVASIVE PROCEDURE SOLELY TO OBTAIN MATERIAL FOR RESEARCH

Normally, it is not necessary to obtain separate consent to obtain research samples as this consent will be given when the research subject is recruited and consents to join the research study. However if the research involves an operative procedure which, if being carried out for therapeutic purposes, would require an operation consent form, then this example operation consent document could be used.

Description of the procedure to be used and the sample to be obtained.

Statement that the procedure is to be done solely to obtain the research sample and that there is no therapeutic benefit to the research subject.

Description of any risks (even remote risks) of the procedure.

Notification that appropriate care will be provided if any adverse events arise during the procedure or a result of carrying out the procedure to obtain the sample.

I give permission for the procedure of

To obtain a sample of

For research

Signed

I have explained the risks of the invasive procedure. I have explained that this procedure is of no therapeutic benefit but is being done solely in order to collect the research sample.

Signed

Appendix C

EXAMPLE CONSENT DOCUMENT FOR VARYING A ROUTINE INVASIVE PROCEDURE TO OBTAIN MATERIAL FOR RESEARCH

Where a variation in a normal surgical technique is to be performed in order to obtain the research specimen, and where the specimen would not normally be removed as part of the therapy, then the following supplementary consent should be obtained in addition to the standard operation consent form.

Description of how the surgical technique will vary from the normal planned surgical procedure.

Description of the sample to be obtained.

Description of any additional risks (even remote risks) that are extra to the normal risks of the planned surgical procedure.

Description of care to be provided in event of a side effect.

I give permission for a sample of
to be collected for research purposes during the operation of.....

Signed

I have explained the variation in the normal surgical procedure required to collect the research sample. I have reviewed the additional risks of the variation in the normal procedure, over and above the normal risks of the planned surgery and the care to be provided if side effects occur. I have informed this patient that giving or withholding consent for obtaining the research sample will make no difference to the planned therapeutic surgery and subsequent follow up care and treatment.

Signed

Doctor/ surgeon who will undertake the surgical procedure.

Appendix D

**CONSENT FOR USE OF HUMAN BLOOD, BODY FLUIDS
OR TISSUE GIVEN FOR RESEARCH**

I consent to use of my specimen of(e.g. blood, urine, etc.) for the following research project.

Name of project

If any of my specimen is left over after this research project has been completed:

1. I wish this left over specimen to be destroyed immediately ★

OR

2. I give permission for the left over specimen to be kept for future research on condition it is **not** used for the following types of research:
.....
.....

and

is destroyed after the following period of time

and

my identity has been removed from the specimen ★

or

my identity is kept with the specimen. ★

OR

3. I give permission for the left over specimen to be kept for future research that is:

related to the medical condition that is the subject of this study ★

or

related to the following health conditions ★

4. I give permission for the left over specimen to be kept for future research of any type and at any time on the understanding that:

my identity has been removed from the specimen ★

or

my identity is kept with the specimen. ★

Name

SignatureDate.....

★ The research subject should initial the boxes of their choice.