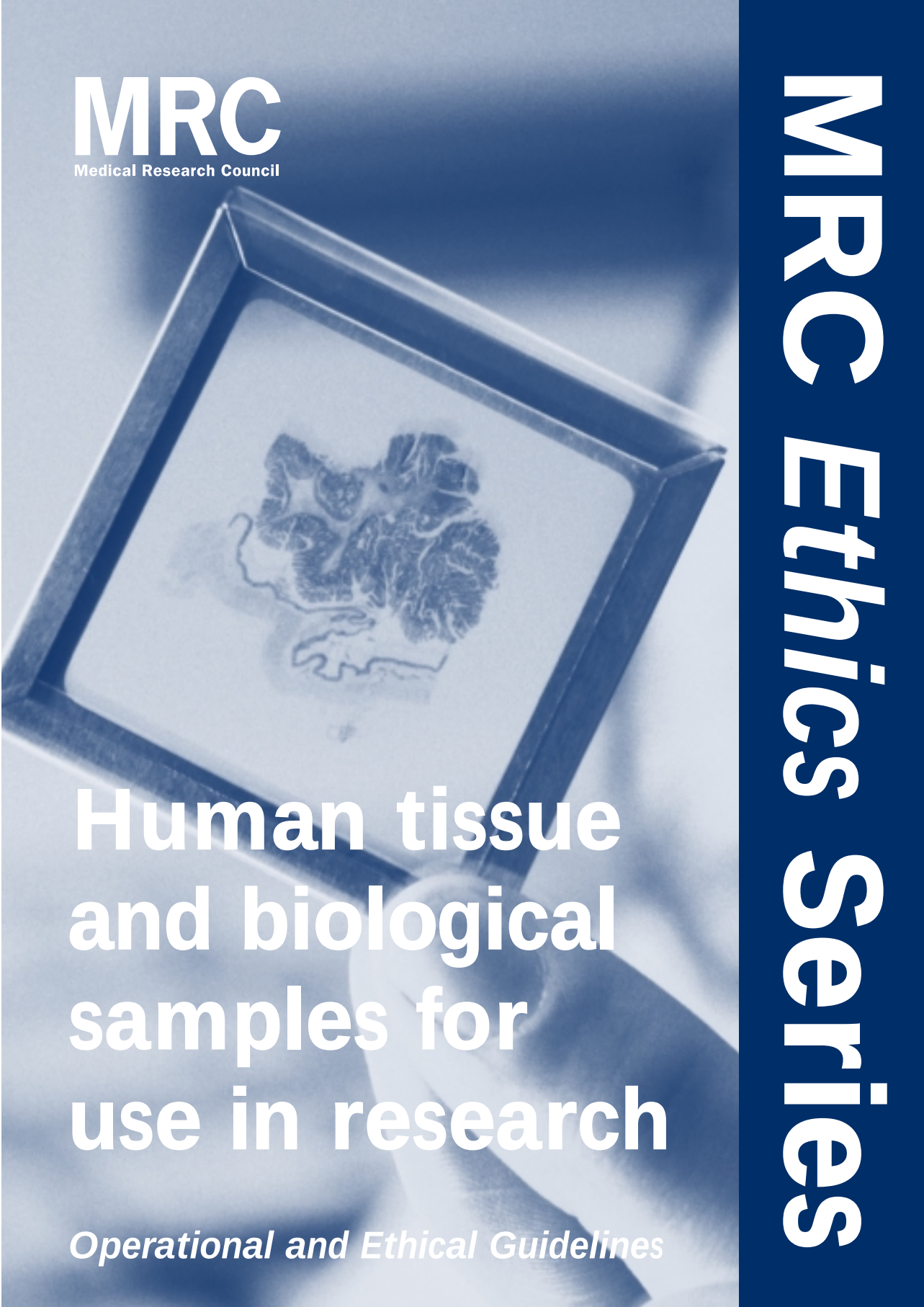


A hand is holding a glass slide with a tissue sample, which is being viewed under a microscope. The background is a soft, out-of-focus blue.

Human tissue and biological samples for use in research

Operational and Ethical Guidelines

MRC Ethics Series

HUMAN TISSUE AND BIOLOGICAL SAMPLES FOR USE IN RESEARCH

The members of the Working Group that developed these guidelines were:

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Updates to this guidance are available on MRC's website: www.mrc.ac.uk

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FOREWORD

Several factors led the MRC to decide that there was a need to develop guidance for researchers on ethical, legal and management issues relating to the use of samples of human biological material for research. Technical advances, for instance in the ability to extract genetic material, meant that the potential to use old samples for research was increasing. We were regularly being asked for advice on what should happen to potentially useful sample collections when a research team disbanded or a lead researcher retired, and on what research would be permissible using stored samples originally collected for another purpose. Also it was clear that, following on from rapid developments in knowledge of the human genome sequence, large numbers of well documented human DNA samples would be essential for the research needed to translate this knowledge into real benefits for public health and health care.

In view of widespread concern about informed consent, confidentiality and ethical issues relating to genetic research, we felt it was essential to establish the general principles that could govern the use of all human biological material in research, including DNA.

The use of human biological material is critical for medical research. Consequently, the public and research participants should have confidence that researchers will handle and use such material sensitively and responsibly. It is likewise important to the MRC to ensure that collections of human biological material can be used optimally for research to benefit health. Since our responsibility as a public body is to ensure that our funds are used wisely, we do not want to fund the unnecessary collection of new material. Also, it is unethical to ask people to donate new

samples when the research questions could be addressed using existing samples.

These guidelines were developed by a Working Group that included members with expertise in law and ethics as well as medical research. They, along with their interests, are listed at the front of the document. Working drafts of the guidelines were sent out for consultation to a wide range of organisations and individual scientists with an interest in the use of human material in research. Their comments were taken into account in developing an interim version, which was then published, together with a more detailed report of the working group's discussions, for wider public consultation and input. Comments were received from Research Ethics Committees, from researchers, patient and consumer groups, and from the MRC's Consumer Liaison Group.

Safety and protection from potential biological hazards are clearly important issues for researchers handling samples of human material, but were not within the remit of the group and are not addressed in these guidelines.

The guidelines are intended to be short and easily readable: the aim is therefore to set out general principles that can be applied in most situations rather than to cover every possible eventuality. It became clear from the consultation that views vary widely, and MRC will keep this guidance under review in the light of ongoing public debates about some of the key issues, and the work of the Human Genetics Commission, the Nuffield Council on Bioethics and the Council of Europe. This guide, as with other MRC ethics guides, is available on MRC's website at www.mrc.ac.uk, and changes will be highlighted there as they arise.

GLOSSARY

Anonymised samples or data have had any identifying information removed, such that it is not possible for the researcher using them to identify the individual to whom they relate. The term is used in these guidelines to refer to both linked and unlinked anonymised data and samples.

- **Linked anonymised samples or data** are fully anonymous to the people who receive or use them (e.g. the research team) but contain information or codes that would allow others (e.g. the clinical team who collected them or an independent body entrusted with safe-keeping of the code) to link them back to identifiable individuals.
- **Unlinked anonymised samples or data** contain no information that could reasonably be used by anyone to identify the individuals who donated them or to whom they relate.

Coded samples or data have a coded identification to protect the confidentiality of the individual during routine use, but it is possible for the user to break the code and thus identify the individual from whom they were obtained.

Custodianship: Responsibility for safe keeping of samples and control of their use and eventual disposal in accordance with the terms of the consent given by the donor. Custodianship implies some rights to decide how the samples are used and by whom, and also responsibility for safeguarding the interests of the donors.

Genetic research: Investigation of variation in the nuclear or mitochondrial DNA that forms the genome of an individual and may be inherited from parent to child. This may involve direct analysis of DNA or analysis of gene products.

Genetic testing: Tests to detect the presence or absence of, or alteration in, a particular gene, chromosome or gene product, in order to provide diagnostic or predictive information in relation to a genetic disorder. (Such testing does not necessarily require the use of genetic technology.)

Human material: All biological material of human origin, including organs, tissues, bodily fluids, teeth, hair and nails, and substances extracted from such material such as DNA or RNA.

Human tissue or sample collection: Any samples of human biological material to be kept for reference, teaching or future research use.

Existing collections: collections comprising samples that were collected and stored before these guidelines came into operation.

Personal information: all information about individuals, living or dead. This includes written and electronic records and information obtained from samples.

SUMMARY OF KEY PRINCIPLES

Much medical research depends on the use of samples of human biological material. This material often provides the best way of studying human biology and human disease, and appropriate use of such material reduces the need to use animals in research. Material for research may be from healthy people, from patients or from people who have died. Researchers may ask volunteers to donate material (e.g. blood samples) specifically for research, or may use material left over after diagnostic testing or surgery. Samples stored for one purpose may later prove useful for research that was not envisaged at the time the samples were taken.

The following principles should guide all MRC funded research using samples of human biological material.

Research should only go ahead if the potential benefits outweigh any potential risks to the donors of the samples. The physical risks involved in donating samples for research will usually be minimal, but the risk that information from laboratory tests on a sample might harm the donor or their interests must not be forgotten.

The human body and its parts should be treated with respect. Researchers should ensure that they are aware of cultural or religious differences in the meaning and significance attached to the body or specific parts of it before approaching potential donors.

Samples of human biological material obtained for use in research should be treated as gifts. Researchers have a responsibility to

ensure the donors' wishes are respected when using the material.

The human body and its parts shall not, as such, give rise to financial gain. Researchers may not sell for a profit samples of human biological material that they have collected as part of MRC funded research, and research participants should never be offered any financial inducement to donate samples. Payment of reasonable expenses or costs is however acceptable. Donors should be informed if their samples might be used in commercial research. Intellectual property rights (IPR) arising from research using human samples may be sold or licensed in the same way as other IPR.

Informed consent is required from the donor (or the next of kin, if the donor has died) whenever a new sample is taken wholly or partly for use in research. Donors should understand what the sample is to be used for and how the results of the research might impact on their interests. Consent must also be obtained for storage and potential future use of samples.

Patients should always be informed when material left over following diagnosis or treatment (described as surplus to clinical requirements) might be used for research. Wherever practicable, and always when the results of the research could affect the patient's interests, consent should be obtained to the use of such surplus material.

All research using samples of human biological material must be approved¹ by an appropriately constituted research ethics

¹ Although Research Ethics Committees are advisory bodies, they do have to come to a favourable view of each research project before it can begin; we therefore adopt the commonly used term *ethics committee approval* in these guidelines.

committee. This is an important way of ensuring that the interests of the donors are safeguarded.

Researchers should treat all personal and medical information relating to research participants as confidential. This applies as much to the results of laboratory tests done as part of the research project as to information obtained directly from donors or from their medical records. People who donate samples for research must be told what personal or medical information about them will be used in the research, who it might be shared with, and what safeguards are in place to protect their confidentiality.

Research participants have a right to know individual research results that affect their interests, but should be able to choose whether to exercise that right. Researchers must decide at the beginning of a project what information about the results of laboratory tests done on samples should be available to the participants, and agree these plans with the Research Ethics Committee. If research results have immediate clinical relevance, there is a clear duty of care to ensure the participant is informed.

1 Introduction

1.1 Purpose

The Medical Research Council is committed to the highest ethical standards in medical research, and to ensuring that optimum use is made of the public funds it administers. These guidelines draw attention to the practical, ethical and legal issues that should be considered when collecting and using samples of human biological material for research, and address how such material should best be used to increase scientific understanding for the benefit of human health.

These guidelines should be followed by:

- Those preparing research proposals for support by the MRC that include the collection of new samples of human biological material.
- Those planning, undertaking or collaborating in research funded by the MRC, using stored samples of human biological material, whether the samples were collected by themselves or by others.
- Those managing collections of human materials made with MRC funding, or research using such collections.

We hope they might also be of interest to others collecting or using human material for research, as well as to research ethics committees, to research participants and to members of the public.

This guidance applies to the use of samples of human biological material for research purposes. It is not intended to cover the use (or re-use) of human samples for clinical diagnostic purposes, clinical audit, disease surveillance or quality control of existing diagnostic testing procedures².

The principles in these guidelines must be applied to all new samples of human material obtained wholly or partly for use in medical research, whether to be used immediately or to be stored for future use. However, it is acknowledged that it will not always be possible to apply them retrospectively to samples stored before the guidelines were issued. MRC recognises that many existing collections of human material are immensely valuable for research, and that using these collections may be ethical, and in the interests of both patients and the public. Research Ethics Committees have a crucial role in ensuring that they are used in a responsible and ethically acceptable way that is not against the donors' interests.

1.2 Ethical principles

The general ethical principles for research involving human participants are set out in the Council's booklet "Responsibility in investigations on human participants and material and on personal information". The known and potential risks and benefits of the research to the participants and the potential benefits to others must be evaluated and research should only proceed if the potential

² See *Guidelines on the practice of ethics committees in medical research involving human subjects 3rd edition*, (1996, Royal College of Physicians of London) Section 6, for a discussion of the distinction between research, clinical practice and audit.

benefits outweigh any associated risks. The interests of research participants should always take precedence over those of science and society. In most circumstances research can only be done with the full and informed consent of the individual participants, and confidentiality of participants must be maintained. An important principle underlying use of any human material for research should be respect for the human body and for the known wishes of the donor of the material. Researchers must always ensure that their use of human material will not compromise the interests of the donor.

1.3 Special issues relating to collections of human material

Human biological material is very important in medical research. Efficient and well-coordinated use of such material can promote scientific advance and reduce both the research demands on patients and the need to use animals. The MRC wishes to promote better use of valuable material by ensuring that it is easier for other scientists to use it, where appropriate. There are, however, special issues in relation to samples of human material:

- Samples can be stored for a long time, and may be of considerable value for research that was not, and could not have been, envisaged at the time the material was obtained.
- Using material for studies not specifically foreseen at the time it was obtained raises difficult ethical issues in relation to consent.

- It is often either not possible or not practicable to go back to the donors for new consent.
- Information obtained from research using biological samples can have implications not only for the individual donor but also for their relatives, and may sometimes have the potential to lead to discrimination in employment or other areas of life, if disclosed.

In addition, the value of many samples of human material for research depends upon the related clinical or personal information; respect for the confidentiality of information about the donor is therefore important. A parallel booklet in the MRC Ethics Series “Personal Information in Medical Research” gives more detailed guidance on this issue.

1.4 Different types of human biological material used in research

Samples of human material for use in research may be obtained from healthy volunteers, from patients or from people who have died. There are also many types of human material used in medical research, ranging from whole organs or large pieces of tissue, such as surgically removed tumours, to very small samples of blood or urine. The importance and meaning people attach to the donation and use of such samples, and the ethical and practical considerations may differ widely in different circumstances. The main distinctions drawn in these guidelines are between:

- Research on new collections and research re-using stored samples
- Material obtained from living donors and material taken from people who have died
- Human material donated solely or partly for research and material left over following diagnosis or treatment (described as 'surplus to clinical requirements' in these guidelines).

General issues applying to the collection and use of all types of human material are considered first, followed by sections dealing with specific issues. This guide does not give detailed advice on the use of human sperm, eggs or embryos. Use of such material is subject to the Human Fertilisation and Embryology Act (1990) and must be approved by the Human Fertilisation and Embryology Authority.

2 Ownership and Custodianship

- 2.1** The legal position in relation to uses of human tissue was discussed in detail in the Nuffield Council on Bioethics Report “Human Tissue: Ethical and Legal Issues” (1995). In the UK it is not legally possible to own a human body. The law is unclear as to whether or under what circumstances anyone can legally “own” samples of human biological material or whether donors of biological material have any property rights over “their” samples. For human material used in research, the important consideration is not legal ownership, per se, but who has the right to control the use made of samples or their transfer to a third party. Therefore in these guidelines we use the term “custodianship” rather than ownership, to imply responsibility for safe storage of samples, for safeguarding the donors’ interests, and for the control of use or disposal of the material.
- 2.2** We recommend that tissue samples donated for research be treated as gifts or donations, although gifts with conditions attached. This is preferable from a moral and ethical point of view, as it promotes the “gift relationship” between research participants and scientists, and underlines the altruistic motivation for participation in research. It also provides a practical way of dealing with the legal uncertainty over ownership, in that any property rights that the donor might have in their donated sample would be transferred, together with the control of use of the sample, to the recipient of the gift. Gifts may be conditional (that is, a donor may specify what the recipient can do with a gift), and it is very important that the donor understands and agrees to the proposed uses of the donated material. The assumption by the donor is that nothing will be done that would be detrimental to his or her interests, or bring harm to him or her.
- 2.3** If samples taken for research are to be treated as gifts, there must be a recipient, to whom formal responsibility for custodianship of a donated sample of material is transferred. While the principal investigator should have day-to-day responsibility for management of a collection of human material, the MRC considers that it is more appropriate for formal responsibility for custodianship of collections of human material to rest with institutions rather than with individual researchers. This provides greater security for valuable collections, provides better assurance that donors’ rights will be protected and makes it easier to deal with changes in individual circumstances of the principal investigator(s). The university, hospital or other host institution where the principal investigator is based will usually be the most appropriate body to have formal responsibility for custodianship of human material donated for research, but occasionally the MRC will wish to retain custodianship of collections that it funds (see 2.6 below). When central banking facilities are available, there may be a requirement for the investigator to split the sample and provide a portion to the bank as a condition of research funding. Valid consent from the donor will of course be required to share a sample with other researchers in this way.
- 2.4** When consent is obtained, the donor (or the person giving consent in the case of material obtained after death) needs to understand that he/she is making a donation of the sample for use in research. They must be clear who will be

responsible for custodianship of the sample and of any personal or confidential data related to the sample, and what it will be used for.

2.5 The Council of Europe Convention on Human Rights and Biomedicine states that “The human body and its parts shall not, as such, give rise to financial gain”, and the MRC fully supports this principle: the sale of human biological samples for research is not ethically acceptable. Therefore, while reasonable expenses (e.g. travel expenses) may be reimbursed, research participants should never be offered any financial or material inducement to donate biological samples for research. Also, researchers may not sell for profit (in cash or in kind) samples that they have collected with MRC funding. Recovery of reasonable costs, based on a standard accounting system is, however, acceptable. A clear distinction can be drawn between samples of human material and intellectual property rights arising from research making use of such samples. Such intellectual property may be sold or licensed in the usual way.

2.6 For all new collections of human biological materials funded by the MRC, researchers and their host institutions must reach agreement with the MRC on specific arrangements for the custodianship and control of use of sample collections (both while the project is ongoing and after it is finished) before funding is released. For large sample collections with contributions from many clinical centres, and for collections set up with the intention from the outset of providing a research resource, the MRC may wish to retain formal responsibility for custodianship of the collection. In the case of jointly funded collections, arrangements for custodianship will be negotiated with the other funding organisations. We understand that custodianship brings with it the right to determine what happens to a collection after the original project funding is finished, but also the responsibility for its subsequent maintenance. The MRC will normally delegate day-to-day responsibility for management of sample collections to the principal investigator of the research project and their host institution.

3 Use of human material surplus to clinical requirements for research

- 3.1** Tissue or organs removed in the course of surgical treatment or excess human material left over after diagnostic testing can be of considerable value for research and teaching and are widely used for such purposes. However, there is currently little public awareness of this practice, nor indeed of what normally happens to such material if it is not used for research. In a legal analysis, such human material might be considered to have been “abandoned” by the patient and therefore available for use however the surgeon or pathologist sees fit. There is some evidence that people do view use of such material in a rather different light from samples donated specifically for research purposes, adopting the position that it is better that the material should serve some useful purpose than simply be disposed of. However, it would be wrong to assume that such a view is universal, and MRC recommends that wherever practicable individual consent should be obtained for the use for research of human material surplus to clinical requirements. At the very least, for example, patients should be made aware in any surgical consent form that they sign that surplus material may be used for research, and be given the opportunity to refuse. Patients need sufficient information to understand how (if at all) the research might affect their interests, and how their confidentiality will be protected. Where surplus material is to be used in a way that allows research results to be linked to the individual patient, individual informed consent must be obtained if there is any possibility that such results might affect the patient's interests.
- 3.2** It is acceptable to use human material surplus to clinical requirements for research without consent if it is anonymous and unlinked. An example is the use of surplus diagnostic samples for screening to establish the prevalence of an infectious disease such as hepatitis or HIV. Information from such studies is very valuable not only for research but also for public health or health service planning purposes, and provided there is no possible way to link the results of tests to identifiable individuals their interests cannot be compromised. While it is not necessary to obtain individual written consent for anonymised unlinked research, it is good practice to ensure that patients are informed that their samples may be used for research once all clinical requirements have been fulfilled, for example by a clearly displayed notice to that effect.
- 3.3** All research using human material surplus to clinical requirements must be approved by an ethics committee, whether or not the samples can be linked to identifiable individuals. This is an important way of ensuring that patients' interests are safeguarded.
- 3.4** There must always be explicit separation of the consent to the treatment or diagnostic test from the consent to the use of surplus tissue for research. It should be clear to patients that refusal to allow surplus material to be used for research will not affect their treatment in any way. It is also important to make clear to patients what will happen to the surplus material if they do not give consent for its retention for research or teaching.

- 3.5** If individual written consent cannot be obtained, research using samples of material surplus to clinical requirements is only acceptable if the results cannot affect the patient's or their family's interests. The patient must also have been informed at the time the sample was taken that their material might be used for research, for example by clearly displayed notices, by distribution of leaflets, or on the clinical consent form itself.

4 Use of human material for commercial research

- 4.1** The MRC's mission is to support research that will ultimately benefit human health. The development of new drug therapies, and diagnostic and screening tests, to the point where they can be made sufficiently widely available to benefit human health, is crucially dependent on commercial involvement. Therefore access by the commercial sector to samples of human material collected in the course of MRC-funded research should be facilitated, where this is consistent with our mission. However, it is NOT appropriate for any one company to be given EXCLUSIVE rights of access to a collection of samples made with the benefit of public funds, nor is it acceptable for any individual to profit financially from providing samples of human material to a third party.
- 4.2** One of the major concerns in allowing commercial access to human material originally collected for research projects funded by the public or charity sectors is the potential to damage the gift relationship between scientists and research participants. Research participants may be particularly sensitive to the idea of a company or an individual making a profit out of research material that they have freely donated. It is important that research participants are made aware of the potential benefits of allowing commercial access, and that the role of any one individual's sample in the generation of future profits is likely to be minimal as well as impossible to quantify. Given the possible sensitivities, it is essential that research participants know that their sample or products derived from it may be used by the commercial sector, and that they will not be entitled to a share of any profits that might ensue.
- 4.3** It is important to distinguish between the samples themselves and the data or intellectual property derived from research using them. Exclusive access to data arising directly from a company's experiments for sufficient time to secure patent protection or other commercial advantage is acceptable, as is ownership by a company of any intellectual property rights arising from their own research using samples of human material.
- 4.4** Patenting of inventions based on, or using, biological material of human origin is covered by the EU Directive on the Legal Protection of Biotechnological Inventions. To comply with the Directive, a person from whose body the material used for an invention is taken must have had an opportunity of expressing free and informed consent (Recital 26). This should be borne in mind when there is a possibility that human material collected for research may be used directly in making a biotechnology product. For instance, if a cell line is to be made and used for commercial purposes the donor must be consulted and consent obtained.
- 4.5** Custodians of collections of human biological material should ensure that a written agreement covering access to data and ownership of intellectual property rights is secured before allowing access to samples by either commercial companies or academic researchers.

5 Confidentiality

5.1 In many cases the use of human material in research also involves the use of personal or clinical information related to the individual who donated the sample. Tests done on the material may also give rise to information about the individual donor. Doctors and researchers should treat any information about an individual, however derived, as confidential. This is what the public expects, and is underpinned by the duty of confidentiality in Common Law, and in Data Protection legislation. Both the data collected from individuals or their medical records to characterise samples in a collection, and data derived from experiments done on those samples, are covered by the Data Protection Act (1998), so long as they can be linked to an identifiable individual. Researchers must ensure that their registration under the Act covers all their uses of data related to samples.

5.2 Detailed guidance on confidentiality is available in the MRC booklet “Personal information in medical research” (see box for a summary of the key points) and in the General Medical Council guidelines on confidentiality. People who donate samples for research must be told what information about their medical history or other personal details will be used in the research, who it might be shared with, and what safeguards are in place to preserve confidentiality. They should give explicit consent to these arrangements.

Key principles of the MRC guidance on personal information in medical research

- Personal information provided for health care or medical research is confidential. Wherever possible people should know how information about them is used. Researchers should normally have each person's explicit consent to obtain, store and use information about them.
- All medical research using identifiable personal information or anonymised data from the NHS that is not already in the public domain must be approved by a Research Ethics Committee.
- All personal information must be coded or anonymised as far as is possible and as early as possible in the data processing.
- Each individual entrusted with patient information is personally responsible for their decisions about disclosing it. Personal information should only be handled by health professionals or staff with an equivalent duty of confidentiality.
- Principal investigators have personal responsibility to ensure that procedures and security arrangements are sufficient to prevent breaches of confidentiality.
- At the outset researchers must decide what information about the results should be available to the people involved, and agree these plans with the Ethics Committee.

5.3 Data that have not been anonymised should not be transferred without informed consent. The responsibility lies with the custodian to ensure that all data related to samples of human material are unidentifiable before release to other researchers or inclusion in a common database. It is good practice to store, process and analyse personal data in a form that does not allow individuals to be identified. Personal information should only be accessible to staff who have a formal duty of confidence to the research participants. Researchers handling personal information should have a duty of confidence to research participants included in their contract of employment. In addition, identifiable data should not be transferred to a country outside the European Economic Area unless it has an equivalent data protection regime.

5.4 Users of anonymised samples of human material must undertake not to attempt to identify individual research participants, and individuals, families or groups should not be identifiable from published data. Any renewed contact with donors not specified in the original research protocol (for example, if

it is necessary to collect additional information) requires further ethics committee approval. This contact must be via the original researcher responsible for making the collection or the current custodian of the samples, and at their discretion.

5.5 The value of a collection for research will usually be significantly increased if all the data relating to the samples are stored together and made available in an anonymised form to all users. Custodians of collections of human material are encouraged to make it a condition of access to the samples that copies of all data generated by other users are provided to the custodian for inclusion in a common database. A suitable period of exclusive access may be allowed, to give sufficient time to analyse the data and prepare publications. The requirements of confidentiality and data protection must of course be met. This sharing of data is an essential requirement where sample collections are being managed as a resource for multiple users.

6 Consent

6.1 The General Medical Council guidelines “Seeking patients’ consent: the ethical considerations” include general advice on seeking consent for research. When obtaining consent to take a sample of biological material for research, it is important that donors have sufficient understanding not only of the process involved in obtaining the sample and any associated physical risks, but also of what the sample is to be used for and how the results of the research might impact on their interests. Written evidence of consent must normally be obtained, as stated in the GMC guidelines. Written consent is not a substitute for careful explanation. It is simply a means of providing documentary evidence that an explanation of the research has been provided and consent has been sought. In some countries verbal consent is acceptable. There must however always be a written record that consent has been obtained even when the person giving consent is not able to write or when verbal consent is the accepted practice. Signed consent forms or documentary evidence of consent, together with copies of patient information materials, must always be kept for future reference. If the information leaflets are revised in the course of a study, all the new versions must be numbered and kept and details of when the changes were introduced should be recorded.

6.2 When obtaining consent to take a sample of human material for research, it is important to allow for the fact that it might subsequently be useful for new experiments that cannot be foreseen. Therefore, unless a sample will be fully used up for the initial project or cannot be stored, a two-part consent process is recommended, the donor being first

asked to consent to the specific experiment(s) already planned, and then to give consent for storage and future use for other research. Unless the sample is to be anonymised and unlinked prior to storage (in which case this should be explained to donors), it is not acceptable to seek unconditional blanket consent, for example using terms such as ‘all biological or medical research’.

If samples may be stored or used in a form that allows them to be linked to individuals, possible future research should be explained in terms of the types of studies that may be done, the types of diseases that could be investigated, and the possible impact of the research on them personally. The benefits of enabling more efficient use of valuable samples should be explained to donors. For example, a researcher collecting samples from patients with diabetes might seek consent to store the samples for future research into the biological basis and treatment of diabetes and related complications, on the basis that researchers using the sample for secondary research cannot identify the donor. Researchers undertaking a broader epidemiological study might seek consent to store samples for future research into biological or genetic factors affecting the risk of developing a range of common medical conditions, on the understanding that results of tests done for research purposes will not have direct clinical implications for the donor. Similarly, donors must be made aware that other researchers might use their samples, including scientists working for commercial companies (if appropriate). Participants must be given the reassurance that all secondary use will require approval by an ethics

committee, and that no tests of known clinical value for diagnosing or predicting disease on samples that can be linked to them individually will be done without their consent.

Information for participants should include an explanation of how any surplus material will be disposed of when it is no longer required.

Where a two-part consent process is used, donors must always be given the option of specifying that their sample may only be used for the research project already planned. If consent is obtained to use a newly collected sample for one specific study only, the only purpose for which it can be re-used is to verify the results of that study. When no longer required for that purpose it should be destroyed. It is the responsibility of the custodian to ensure that all uses of a sample are in accordance with the consent obtained from the donor.

6.3 If research using samples will require the collection of information from the donor's medical records, then consent must be obtained. It must be clear who will access the records, what information will be obtained, and how the patient's confidentiality will be protected.

6.4 The special sensitivity of the public with regard to genetics research should always be taken into account. If there is the possibility that secondary use may include genetic research, this must be included in the explanation of possible future research when consent is obtained. There are certain types of genetics research which currently give rise to particular concern, for instance that relating to personality, behavioural characteristics, sexual orientation or intelligence. It is particularly important that specific consent is obtained to

use samples in these or other areas of research likely to cause special concern to the donors, even if the samples are to be anonymised and unlinked.

6.5 When seeking consent for research, information for potential participants must be presented in a form that they can understand. Where lack of ability to understand written information may be a problem, the use of audio taped information is recommended. If potential participants do not speak English, interpreters should have sufficient understanding of scientific and medical issues to explain adequately the aims of a research protocol. These interpreters should preferably be patient advocates or NHS interpreters rather than relatives. If relatives must be involved, they should be competent adults who are themselves fluent in English. Information leaflets should be translated by people with a technical knowledge of the field. Researchers should be aware that members of some ethnic or religious groups might find some types of research, or donation of certain types of human material, unacceptable.

6.6 Particular considerations apply in the case of research involving children (see 12.3) and people who, as a result of permanent or temporary mental incapacity, cannot give valid consent (see 12.4). The Council's guidance on the latter situation is set out in a separate publication³ and there are also guidelines for Research Ethics Committee and guidelines issued by the Royal College of Physicians and by the Royal College of Paediatrics and Child Health (see Appendix 1). A summary of all the issues to be addressed in the process of obtaining consent is at Appendix 3 and a model consent form is at Appendix 4.

³ *The Ethical Conduct of Research on the Mentally Incapacitated MRC Series, December 1991*

7 Ethics Committee Review

Ethics committee approval must be obtained to collect samples of human material for research, and for all research projects using samples of human material. New ethics committee approval is required for all research projects not specifically mentioned when consent was originally obtained or in previous ethics committee submissions. This is an important means of safeguarding the interests of the donors. Ethics committee approval must also be obtained if there is a need to access patients' medical records without their specific consent. This may be justified under certain circumstances: if the study is of sufficient importance, if there are no practicable alternatives, if the infringement of confidentiality is kept to a minimum, and if there is no intent to make future contact with the patient.⁴

⁴ See the MRC Ethics booklet "*Personal Information in Medical Research*" for more detailed guidance

8 Feedback of Information

8.1 Tests done on samples of human material in the course of research may reveal information that has implications for the donors' future health or healthcare, or otherwise impacts on their interests. It is important to decide before the start of a research project what will be done if this arises. Researchers should be cautious about assuming that they, rather than the individuals concerned, are best placed to judge what information is of interest to donors on a case-by-case basis. For instance, some researchers may take the view that information should only be fed back if there is a treatment or preventive intervention available. However, research participants might wish to know predictive information about their future health, even if there is no treatment available, for example to take it into account when making important life decisions, such as whether to have children. Researchers should assume that participants have a right to know information that may affect their interests, but that they might choose not to exercise that right. When participants are asked to make a decision on whether or not they want results to be fed back to them they must be given sufficient information to allow them to decide what their interests are and to make any refusal meaningful. Researchers must decide at the outset what their strategy will be with regard to feeding back information and whether any linkage of research results to individuals will be possible or alternatively whether the unlinked anonymous technique is appropriate. This must be set out in their submission to the ethics committee, and the policy adopted must be explained clearly to research participants before they consent to take part in the research.

8.2 Research results obtained on anonymised unlinked samples cannot have any impact on the interests of an individual donor, and cannot be fed back. Much research can be done using anonymised unlinked samples, and indeed in many instances this is the most appropriate technique. For example, it has been used successfully in research into the spread of HIV infection.

However, irreversibly breaking the link between a sample and the individual donor can undoubtedly reduce its value for some types of research, for instance by making it impossible to add follow-up data or to audit fully the research results. In deciding whether to use anonymised unlinked samples, researchers should take into account the nature of the foreseeable research findings, the importance of obtaining follow-up information on participants, the initial consent obtained and the feasibility of obtaining further consent. The ability to provide feedback linked to counselling and clinical care must also be considered. There are various possible strategies for unlinking: samples can be irreversibly unlinked from the outset, or they can be unlinked after the initial study is done, either before being used for any secondary studies or before use in specific studies only.

8.3 Incidental clinical findings

Where a result that can be linked to an individual has immediate clinical relevance (for example, if it reveals a serious condition for which treatment is required), the clinician involved has a clear duty of care to inform the research participant, either directly or via the clinician responsible for his or her care. The

clinician responsible for care should always be notified, and participants should be informed that this will occur. A research result should not be relied on as the sole basis for diagnosis, since quality control standards in research laboratories generally differ from those used for clinical testing. Research participants or their clinicians should be advised to seek a repeat or confirmatory test by a clinical diagnostic laboratory where possible. Where a confirmatory test is not available via the NHS the diagnosis might need to be verified by the research laboratory using a new sample.

8.4 Research results

There is currently no consensus on whether, or under what circumstances, it is appropriate to feed back research results to participants on an individual basis⁵. Often the clinical relevance or predictive value of a research result is unclear, at least initially, and there will be no individual data of value to be fed back. It will always be difficult to define the point at which a research hypothesis becomes a clinical fact. Where consent is being sought for a specific research project at the time a sample is collected, the potential relevance, if any, of the results for the participant should be explained and the opportunity to receive feedback of individual results should be offered where appropriate. There should be a mechanism in place for participants to change their minds (for instance, a contact telephone number). If feedback is requested, they should be given appropriate instructions about how to notify researchers of a change in their address. Researchers feeding back individual results

must be prepared to explain their significance to the participant and to advise on access to counselling or treatment where indicated.

It is good practice to offer research participants the opportunity to be kept informed about the general results of research projects done using the samples they have donated, though this may not be appropriate in all circumstances. Participants could be informed by posting information on research outcomes on a website, or by offering them the opportunity to receive a newsletter. Where the clinical relevance of research results becomes clear some time after the sample was obtained, or where the results obtained from secondary research may impact on the donors' interests, these routes should be used to inform donors that results of potential interest may be available and offer them the opportunity to receive individual feedback or advice if they wish. Similarly, when new predictive tests of clinical value become available as a result of the research, participants can be informed how to access these tests if they wish.

Where samples may subsequently be used for secondary studies, a mechanism should be put in place to allow participants the opportunity to seek individual results that might impact on their interests. It is acceptable for the onus to be on the participant to seek the information rather than on the researcher to be pro-active in providing it. The research protocols for secondary studies and the arrangements (if any) for feeding back results to participants must be reviewed by an ethics committee,

⁵ *The MRC will be monitoring the debate in this contentious area and expects that the position will evolve as a result of ongoing consultation and research*

preferably the committee that oversaw the making of the collection. If samples from a collection are shared with other researchers, the custodian of the collection is responsible for all contacts with donors, including providing any information on research results with a possible impact on individuals.

8.5 Specific issues related genetic research

Much genetic information obtained for research purposes is of unknown or uncertain predictive value. Genetic tests of known clinical or predictive value should not be done on samples that can be linked to an individual without their specific consent, and appropriate counselling should be available if consent for such a test is sought. Participants should be advised of the possible implications of genetic information for other family members and the potential impact on family relationships, and also of the implications of genetic risk information for employment or their ability to obtain insurance, before they decide whether to give consent to the test or whether they want to know the result. The feeding back of other genetic information, the significance of which is currently unknown, could also have similar implications in the future. The Advisory Committee on Genetic Testing guidance to Research Ethics Committees gives more detailed advice on feedback in relation to genetic information (see Box).

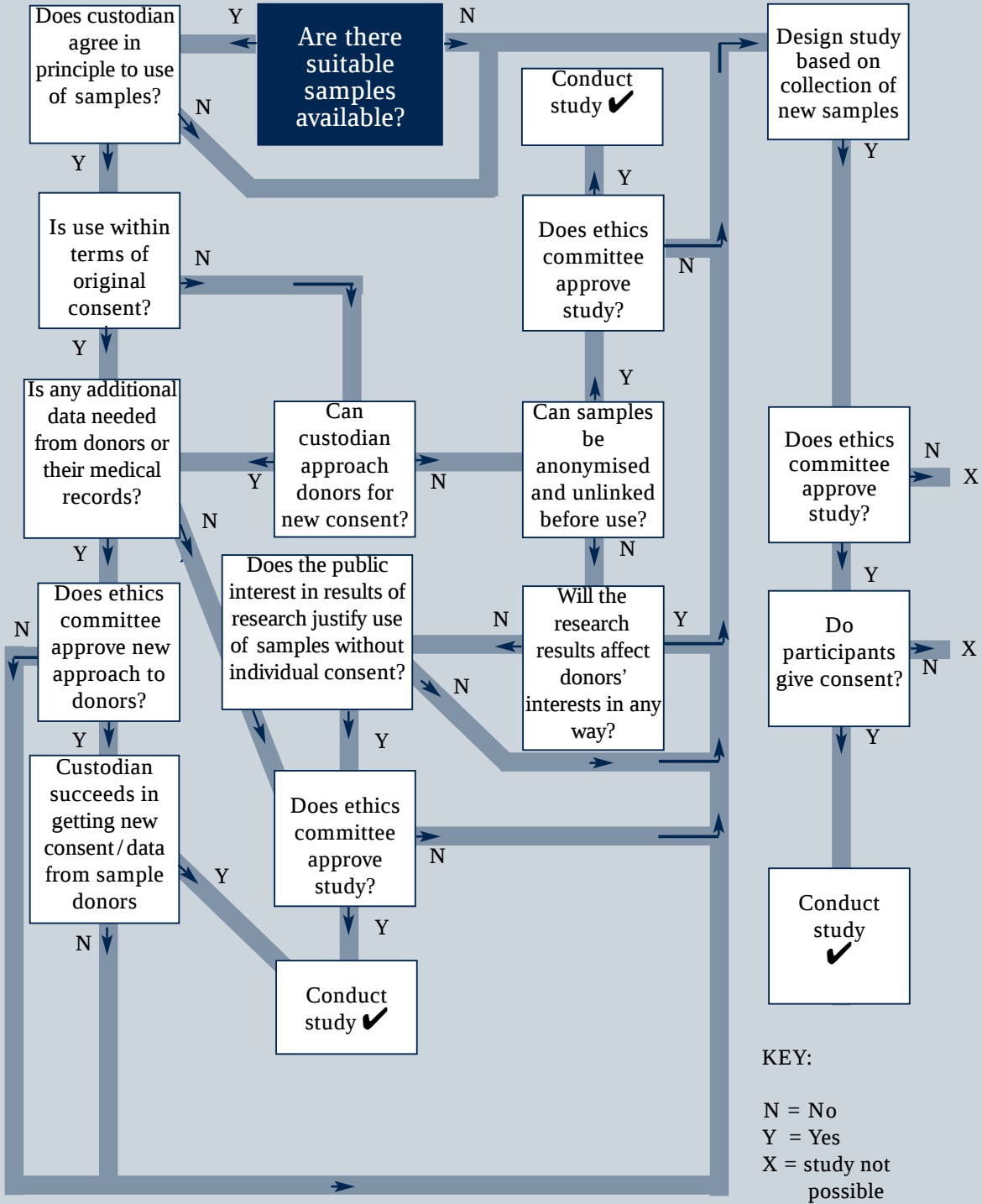
Summary of ACGT guidance on feeding back genetic information.

- Whenever practical there should be a clear distinction between diagnostic testing and research. If a research participant later requests a test for clinical purposes a new sample should be taken.
- Genetic testing should not be added to an existing research study without consent.
- Unless samples are anonymous and unlinked, prior consent must be obtained for each genetic test carried out for research purposes.
- If genetic test results are to be disclosed to research subjects or added to their medical record, then informed consent is required for the tests. It must be clear what use may be made of test results and subjects must be fully informed of potential adverse consequences for insurance, employment and effects on family members.
- The fundamental issues of information, consent and confidentiality are the same for research involving multiple gene tests, such as genotyping. Researchers should establish suitable methods by which complex information about the research can be explained to participants.

9 Management of collections of human material

- 9.1** The MRC reserves the right to specify the arrangements for management and access of sample collections as a condition for awarding funding. In the case of jointly funded collections, these arrangements would be negotiated with the other funders. This will allow us to ensure that collections are managed appropriately to maintain their usefulness, and to ensure that optimum use is made of them.
- 9.2** The MRC wishes to promote sharing of useful collections with bona-fide academic researchers undertaking high-quality research, provided that appropriate consent has been obtained and that such use is not against the interests of the donor. Use of samples by third parties must be on terms that do not disadvantage those involved in making and maintaining the collection or unnecessarily hamper or restrict future uses. The onus is on the custodian of a collection of human material to facilitate optimum usage; this will usually mean undertaking to provide access to other researchers once the requirements of the original project have been satisfied. In the case of collections made for a specific research project, it will usually be appropriate for the investigators making the collection to have priority access and the right to control use of the collection for the duration of the initial study.
- 9.3** For large collections, and those set up specifically to provide a resource for multiple users, requests for access should usually be dealt with by a management committee, which should have an independent chair and some independent membership. Criteria for access should be agreed at the outset. For example, proposed research should be subject to peer review as a means of ensuring scientific quality, samples and associated data should only be used for purposes approved by the committee, and researchers should agree to put all new data into a common dataset. Where supplies of samples are limited, transparent arrangements for prioritising requests for access are essential. Proper records of sample distribution must be kept and users must agree to return or destroy material surplus to their requirements and not use it for additional studies or pass it on to others. The management committee should also be given copies of all papers describing research using the collection before publication (but should not have the right to delay or veto publication).
- 9.4** Custodians of samples of human biological material are responsible for keeping proper records of all uses that have been made of the material, whether by themselves or by others. They must also ensure that all uses have appropriate ethics committee approval, and keep copies of such approvals for reference. Where linked anonymous samples are provided to a third party, the custodian is responsible for safe keeping of the code enabling samples to be linked to individual donors.

Figure 1 - Using established collections in research - a decision tree



10 Established collections

10.1 Custodianship, management and access

It is important to assess periodically whether old samples of human material should be kept, taking into account both their scientific value and ethical issues. If samples are no longer of value, they should be disposed of safely and sensitively. For many old collections, no specific arrangements for custodianship of samples and management of access will have been put in place. This can present problems when researchers retire or move to a different job, or when there is disagreement over who should be allowed to use the samples. When a researcher wishes to move samples to a new location, the agreement of the current and the future host institution must be sought, and contributors to the collection must be consulted where possible. When a researcher retires and sample collections are to be retained, the institution or department should ensure arrangements are put in place for future maintenance and management, and that a new person is identified to take on responsibility for the collection. Custodians of established collections are encouraged to ensure that they are used optimally, and to allow access to other researchers wherever practicable, provided this is consistent with the consent that was obtained and confidentiality is not breached.

10.2 What research can be done using old samples?

There are many potentially valuable collections of human samples for which consent was only obtained for a single research project, or for which information on the parameters of the consent obtained has not been adequately recorded. Generally, established collections can be used for research when samples have been anonymised, and there is no potential harm to the donors of the material, individually or as a group⁶. Researchers should satisfy themselves that the samples were not obtained in an unethical or improper way and that there was valid consent to the taking. The HUGO Ethics Committee “Statement on DNA sampling: control and access” specifies the circumstances under which it is acceptable to do genetics research on archived samples. This suggests that such research is permissible on coded samples. The MRC believes that where a genetic test is of known predictive value, or gives reliable information about a known heritable condition, samples must be anonymised and unlinked before testing unless specific consent is obtained⁷. Even when a donor has died, genetic test results can have implications for surviving relatives. If the predictive value of the genetic information to be obtained is not known, research on anonymised linked samples is permissible, provided there is a strong scientific justification for not irreversibly anonymising the samples (for example, the need to link new information on clinical outcomes to genetic information).

⁶ “Research based on archived information and samples” 1999 Royal College of Physicians, London

⁷ This principle has been set out in the Advisory Committee on Genetic Testing Guidance to Research Ethics Committees

10.3 When is it necessary to seek new consent?

It is of course necessary to seek new consent when collecting new data from research participants. Consent should also be obtained to access participants' medical records if this was not done when the sample was originally collected. Where samples can be anonymised and unlinked before use, no new consent is required. In some rare circumstances research on linked samples originally taken for another research purpose may be permissible without consent. An example would be epidemiological research where the only practicable approach is to use stored samples and identifiers are needed to link samples and different types of health records. Before stored samples are used in this way researchers must demonstrate that contacting donors to seek consent is not possible or not practicable. Old samples of material surplus to clinical requirements may be used for linked research without specific consent if there is no possibility that the research could affect the patients' interests in any way and if obtaining individual consent is not practicable. Ethics committee approval is essential for all new research using stored samples of human material. Detailed guidance on the circumstances under which access to medical records without specific consent may be acceptable can be found in the Ethics booklet "Personal Information in Medical Research". In NHS institutions, the designated "Caldicott Guardian" must approve the use of confidential information.

11 Samples obtained after death

- 11.1** As with other research using human material, ethics committee approval is required for research involving the collection or use of material obtained after death. Before removing and retaining human material for research at a post-mortem examination, all reasonable steps must be taken to ascertain that the deceased would not have objected (for example, for religious reasons). Informed consent to the retention of material for research must normally be obtained from the surviving spouse, partner or next of kin. The person asked to give consent should be given clear information about what tissue/organ will be retained, who will be custodian, how long the sample will be kept, what types of research it may be used for and how it will be disposed of when no longer required. Since this consent is being sought at a particularly stressful time, relatives should wherever possible, be given time to reflect before making their decision, and it is particularly important that written information is provided for later reference. Contact details of the research team must be provided in case relatives have further questions or change their minds later. While in this situation there is clearly no possibility of harming the person from whom the material is obtained, some research results (e.g. from genetic studies) may have implications for the surviving family members. The potential implications for relatives of any research to be done using linked samples must be discussed, and they must be given the opportunity to learn about any research results that might impact on their interests.
- 11.2** In the case of post-mortems required by law, the Coroner (or Procurator Fiscal in Scotland) cannot authorise the retention of tissue for research, but can prohibit it, even if consent has been obtained from a relative. Therefore the Coroner or Procurator Fiscal must be consulted before tissue is retained for research.
- 11.3** If no surviving relatives can be traced, and a post-mortem examination is required to establish the cause of death, the person legally in possession of the body (usually the hospital authority or Trust if death occurred in hospital) may authorise the removal and retention of tissues or organs to establish the cause of death. Once the cause of death of that person has been established, the person legally in possession of the body may at present legally authorise the retention of surplus material already removed from the body for research or teaching purposes. However, MRC recommends that tissue or organs should not be removed and retained solely for research purposes (i.e. if not required to establish the cause of death) if it is not possible to obtain consent from a relative or other appropriate person.
- 11.4** In some situations, the request for material will have been discussed with the deceased prior to death and informed consent obtained directly from them. In this instance it is not necessary to seek the consent of the next of kin, but it is important to make sure that they know what material will be retained, by whom and for how long. If they have strong objections these should be respected in spite of the wishes of the deceased.

12 Special circumstances

12.1 Samples obtained from abroad

When obtaining samples of human material from abroad, researchers must be satisfied that they have been ethically obtained. The researcher should obtain from the clinician providing samples written assurance that they were obtained with proper consent in accordance not only with these guidelines but also with guidelines applicable in the country of origin. The recent Nuffield Council on Bioethics discussion document on “Research in Developing Societies” highlights the ethical issues and the report of their ongoing enquiry should be available in 2001.

12.2 Fetal and embryonic tissue

Fetal tissue must be obtained and used in accordance with recommendations of the Polkinghorne report⁸. This specifies that, where tissue is obtained from therapeutic abortions, there must be clear separation between the decision to induce abortion and any decision concerning use. The decision to terminate a pregnancy must not be influenced by consideration of the possible use to which the tissue may be put, and the Polkinghorne report states that no specific references should be made to any particular research use when consent is obtained. This is therefore one situation where consent must be obtained for general research use and not for a particular project. To ensure proper separation is maintained, MRC recommends that researchers needing to use fetal tissue obtain it from one of the established tissue resources that the Council funds. The placenta and other

contents of the uterus are not considered fetal tissue, and consent should be obtained from the mother in the same way as for the use of any other human material. Any research on pre-implantation embryos created as a result of in vitro fertilisation must be approved by the Human Fertilisation and Embryology Authority.

12.3 Children

There are several sources of detailed ethical guidance on research in children (see Appendix 1). Parents with parental responsibility may legally give consent on behalf of a child. When children have sufficient understanding and intelligence to understand what is proposed, they themselves should consent to participation in the research, and it is good practice to seek parental consent also. Where a sample of biological material has been obtained from a young child on the basis of consent from their parent and stored for subsequent research use, and there is ongoing contact (e.g. in longitudinal studies), the child should be asked for consent to continued use of that sample once they are old enough to understand. Tests of known predictive value for adult onset diseases should not be done for research purposes on individually identifiable samples from children⁹.

⁸ *Review of the Guidance on the Research Use of Fetuses and Fetal Material HMSO July 1989*

⁹ *Advisory Committee on Genetic Testing Report on Genetic Testing for Late Onset Disorders 1998*

12.4 Adults not able to give consent

The Council's booklet "The ethical conduct of research on the mentally incapacitated" sets out the conditions that must be satisfied for inclusion of those unable to consent in research. The person must not object or appear to object, and an informed independent person acceptable to the Local Ethics Committee must agree that the individual's welfare and interests have been properly safeguarded. Risk of harm must be negligible (for non-therapeutic research) or must be outweighed by the likely benefits, and the research must not be against the individual's interests.

Researchers should seek the agreement of carers or relatives when seeking the involvement in research of adults that cannot themselves give valid consent, but should be aware that there is no provision in English law for anyone to give consent on behalf of another adult. In Scotland, following the implementation of the Adults with Incapacity

(Scotland) Act (2000), it will be legally possible for a guardian or person with power of attorney to give consent to medical treatment or research on behalf of an adult unable to consent for themselves.

When seeking consent, it is important for the researcher to ascertain whether the potential participant has the capacity to consent. There will be individuals who, while not suffering from mental illness as such are, through grave illness or stress, in a state of altered consciousness or reduced comprehension when samples are obtained. The validity of consent obtained under these circumstances is questionable. If taking samples cannot be delayed, participants must be given full information about the research and the opportunity to withdraw when capacity to give valid consent is regained. If they do not wish to participate in the research their sample and all related data must be destroyed.

Nuffield Council on Bioethics. Human Tissue, Ethical and Legal Aspects. London: Nuffield Council on Bioethics, 1995.

Medical Research Council. Responsibility in investigations on human participants and material and on personal information. London: Medical Research Council, 1992.

Statement from the Royal College of Physicians Committee on Ethical Issues in Medicine. Research based on archived information and samples. Journal of the Royal College of Physicians of London, 33:264-6:1999.

Royal College of Pathologists. Consensus statement of Recommended Policies for uses of Human Tissue in Research, Education and Quality Control - with notes reflecting UK law and practices. London: Royal College of Pathologists, 1999.

Advisory Committee on Genetic Testing. Advice to Research Ethics Committees. London: Department of Health, 1998.

Advisory Committee on Genetic Testing. Report on Genetic Testing for Late Onset Disorders. London: Department of Health, 1998.

The Human Genome Organisation Ethics Committee. Statement on DNA Sampling: Control and Access. London: Human Genome Organisation, 1998.

Royal College of Pathologists. Guidelines for the retention of tissues and organs at post-mortem examination. London: Royal College of Pathologists, 2000.

Royal College of Paediatrics and Child Health. Guidelines for the Ethical Conduct of Medical Research Involving Children. London: Royal College of Paediatrics and Child Health, 1999.

Medical Research Council. The Ethical Conduct of Research on the Mentally Incapacitated. London: Medical Research Council, 1991.

The Wellcome Trust. Guidelines for Issues to be Addressed When Considering Support for Collections of Human Samples. London: The Wellcome Trust, 1998.

General Medical Council. Seeking patients' consent: the ethical considerations. London: General Medical Council, 1998.

General Medical Council. Confidentiality: protecting and providing information. London: General Medical Council, 2000.

Nuffield Council on Bioethics. Mental disorders and genetics: the ethical context. London: Nuffield Council on Bioethics, 1998.

Review of the Guidance on the Research Use of Fetuses and Fetal Material. London: Stationery Office, 1989.

Grubb A. I, Me, Mine: Bodies, Parts and Property. Medical Law International; 3:299: 1998.

The Inquiry into the management of care of children receiving complex heart surgery at the Bristol Royal Infirmary: Interim Report. Removal and retention of human material. <http://www.bristol-inquiry.org.uk>, 2000.

The Royal Liverpool Children's Inquiry: Summary and Recommendations. <http://www.rlcinquiry.org.uk>, 2001.

Doyal L, Tobias J S. Informed consent in medical research. BMJ Books, London, 2000. ISBN 0-7279-1486-3.

Checklist for research based on samples of human material

consent from the next of kin?

Source of samples

- ◆ If new samples are to be collected for this research, will appropriate measures be taken to minimise any risks of physical harm. Could the approach to potential donors cause distress?
- ◆ If samples are to be collected from patients temporarily unable to give consent (e.g. during emergency surgery), are there appropriate arrangements to consult next of kin, to obtain informed consent later and for patients to opt out if they wish.
- ◆ If the research is using samples originally collected for another research project, is the research covered by the consent already obtained? If not, can new consent be obtained from the donors or can the samples be anonymised and unlinked?
- ◆ If the research will use material surplus to clinical requirements, are the patients aware that their material might be used in this way and of their right to object? Would it be practicable to obtain individual consent?
- ◆ If samples are to be obtained after death, is it possible to discuss the study with potential donors and obtain consent before death? If not, are appropriate arrangements in place to get

Justification for the study

- ◆ Could information obtained in the course of the research bring harm or distress to the donors, individually or as a group, or to members of their family?
- ◆ Do the potential benefits of the research outweigh the risks?

Conduct of the research

- ◆ Are adequate measures in place to protect the confidentiality of personal information required for or revealed by the research¹⁰?
- ◆ Is it clear to donors who will have access to their samples or personal information about them?
- ◆ What will happen to the samples after the research is finished? Will appropriate consent be obtained if they will be stored for future use?

Feedback of information

- ◆ Could tests done on the samples as part of the research reveal information of immediate relevance to a donor's health or healthcare? If so, will the donors be made aware of this possibility and are the arrangements for feeding back this information appropriate? Have the arrangements been agreed with the

¹⁰See *Personal Information in Medical Research (2000, MRC Ethics Series)* for a more detailed checklist regarding protection of confidentiality.

people responsible for the donors'
clinical care?

- ◆ Could tests done on the samples as part of the research reveal predictive or other information that might affect the interests of the donor or their family? If so, are arrangements in place to make that information available to donors, and will they have adequate information to make a decision as to whether they want the information? Would it be better if the samples were anonymised and unlinked before testing?
- ◆ Is it clear to participants where they can get information about the outcome of the research?

Summary of issues to address when obtaining consent

3

General guidance on the production of patient information leaflets has been prepared by a working group on behalf of Multi-Centre Research Ethics Committees and is provided to all MREC applicants. This indicates general issues that must be covered for all research studies. In addition, the following specific issues should be covered in the process of obtaining informed consent and in the patient information leaflet for studies in which samples of biological material will be taken from participants. Information leaflets should always meet basic criteria for good quality information provision.

1. For all samples

- ◆ The sample will be treated as a gift.
- ◆ The donor has no right to a share of any profits that might arise from research using the sample.
- ◆ Who will be responsible for custodianship of the sample (host institution/funding body).
- ◆ What personal information will be used in the research.
- ◆ The arrangements for protecting the donor's confidentiality.
- ◆ If the research might reveal any information of immediate clinical relevance, this will be fed back.

- ◆ Arrangements for feeding back or obtaining access to individual research results, if any, and for informing participants of the outcome of the research.
- ◆ Consent to access medical records, if required.
- ◆ Specific consent for any genetic tests, if required.

2. If the sample is to be stored for possible secondary use

- ◆ The types of studies the sample may be used for and the diseases that may be investigated.
- ◆ Possible impact of secondary studies on the interests of donors and their relatives.
- ◆ Means of accessing information on secondary studies, if appropriate.
- ◆ Secondary studies will have to be approved by an ethics committee.
- ◆ Consent to share samples with other users.
- ◆ Consent to commercial use, and an explanation of the potential benefits of commercial involvement, if appropriate.

Model consent form for research involving new samples of human biological material

This form is a model, to be adapted as appropriate to suit particular studies. Sections not required should be omitted, and other sections may be needed if the project involves more than simply collecting a sample.

Host hospital/institution
headed paper

Thank you for reading the information about our research project. If you would like to take part, please read and sign this form.

Centre number:

Study number:

Patient identification number for this study:

Title of project:

Name of researcher:

Contact details for research team:

Please initial boxes

1. I have read the attached information sheet on this project, dated
(version.....), and have been given a copy to keep. I have been able to ask questions about the project and I understand why the research is being done and any risks involved. ☐
2. I agree to give a sample of (blood-afterbirth-tissue-other, as appropriate) for research in this project. I understand how the sample will be collected, that giving a sample for this research is voluntary and that I am free to withdraw my approval for use of the sample at any time without giving a reason and without my medical treatment or legal rights being affected. ☐
3. I give permission for someone from the research team to look at my medical records to get information on (complete as appropriate). I understand that the information will be kept confidential. ☐
4. I understand that (my doctor and/or I, as appropriate) will be informed if any of the results of the medical tests done as a part of the research are important for my health. ☐
5. I understand that I will not benefit financially if this research leads to the development of a new treatment or medical test. ☐
6. I know how to contact the research team if I need to, and how to get information about the results of the research ☐

7. Consent for storage and use in possible future research projects

I agree that the sample I have given and the information gathered about me can be stored by (name of custodian) at the (name of host institution/host institution on behalf of MRC) for possible use in future projects, as described in the attached information sheet¹¹. I understand that some of these projects may be carried out by researchers other than (name of study team) who ran the first project, including researchers working for commercial companies.

☐

8. Consent for genetic research¹²

A: For genetic tests of known clinical and/or predictive value:

I give permission for (name of genetic test) to be carried out on the sample I give, as part of this project. I have received written information about this test and I understand what the result could mean to me and/or members of my family.

☐

I want/do not want (delete as applicable) to be told the results of this test.

I understand I can change my mind about this later.

☐

B: For other genetic research:

I understand that (the project/future research, as appropriate) using the sample I give may include genetic research aimed at understanding the genetic influences on (complete as appropriate) but that the results of these investigations are unlikely to have any implications for me personally.

☐

..... Name of patient (BLOCK CAPITALS)	 Date	 Signature
--	---------------	--------------------

..... Name of person taking consent (if different from researcher)	 Date	 Signature
--	---------------	--------------------

..... Name of researcher	 Date	 Signature
-----------------------------	---------------	--------------------

Would you like to be sent information about the progress of this project? -----	☐ Yes	☐ No
--	---------------------------------	--------------------------------

Form version and date

Thank you for agreeing to participate in this research

¹¹ Participants must be given written information to keep on possible future research - it's goals, the types of tests that are to be done, the diseases that might be investigated, and how the results might affect their interests. The written information should also include an explanation of the safeguards in place to protect their interests, including information on ethical review and how their confidentiality will be protected.

¹² If genetic research may be carried out on the sample then specific consent is required. One or both sections A, or B, should be included in the consent form.



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