The Availability of Human Tissue for Biomedical Research

The Report and Recommendations of ECVAM Workshop 32

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Preface

This is the report of the thirty-second of a series of workshops organised by the European Centre for the Validation of Alternative Methods (ECVAM). ECVAM’s main goal, as defined in 1993 by its Scientific Advisory Committee, is to promote the scientific and regulatory acceptance of alternative methods which are of importance to the biosciences and which reduce, refine or replace the use of laboratory animals. One of the first priorities set by ECVAM was the implementation of procedures which would enable it to become well-informed about the state-of-the-art of non-animal test development and validation, and the potential for the possible incorporation of alternative tests into regulatory procedures.

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1ECVAM — European Centre for the Validation of Alternative Methods. 2This document represents the agreed report of the participants as individual scientists.
dures. It was decided that this would be best achieved by the organisation of ECVAM workshops on specific topics, at which small groups of invited experts would review the current status of in vitro tests and their potential uses, and make recommendations about the best ways forward (1). In addition, other topics relevant to the Three Rs concept of alternatives to animal experiments have been considered in several ECVAM workshops.

The workshop on The Availability of Human Tissue for Biomedical Research was held in Barnsdale, Rutland, UK, on 18–22 May 1998, under the co-chairmanship of Robert Anderson (The International Institute for the Advancement of Medicine, UK) and Michael O’Hare (LICR/UCL Breast Cancer Laboratory, UK). There were 20 participants from six European countries.

The principal aim of the workshop was to formulate a set of guidelines to facilitate the safe, ethical and scientifically valid use of human tissues in research. This report summarises the workshop discussions on the ethical, legal, logistical and safety aspects relating to the supply and use of human tissue for research in Europe, and proposes a number of recommendations to improve the availability of non-transplantable and surplus surgical human tissue for research.

Introduction

For many years, research has been conducted in animals in vivo, despite the difficulties with extrapolating results obtained from animal data to humans (2–4). It is therefore desirable to replace the use of animals, not only on ethical grounds, but also on scientific grounds. Whenever possible, in vitro methods should be used instead of in vivo methods, and for many purposes, in vitro systems employing human tissue would be the most scientifically relevant. The areas of research that would benefit from the use of human tissue are both diverse and extensive, but fundamental improvements would include more-relevant investigations of human disease, subsequent development of therapies, and improved safety testing of agents to which humans are exposed.

The two major potential sources of human tissue for research are non-transplantable tissue from cadaveric donors and surplus surgical tissue from live donors. Non-transplantable tissue from cadaveric donors is tissue which is not suitable for transplantation. A health professional, usually a transplant co-ordinator, approaches the relatives of a deceased patient in order to ascertain whether they are willing for their relative’s tissue to be used for transplantation. If the tissue is not suitable for transplantation, the health professional might ask the relatives if the tissue could be used to support research. Surplus surgical tissue is tissue removed during an operation, that is not required for transplantation or histological examination, and is normally discarded. For example, bone and cartilage are removed during most joint replacement procedures, skin is removed during many plastic surgery procedures, and thoracic and abdominal surgeons remove whole or parts of various visceral organs.

The considerations that apply to the acquisition of human tissue from these two distinct sources can differ widely. For instance, in general, surplus surgical tissue would not be considered for transplantation, and its acquisition for research is likely to be a far less emotive issue than approaching bereaved relatives for permission to use non-transplantable cadaveric tissue.

There are indications from health professionals that tissue which could be used for research is currently being wasted. The reason for this situation is multifactorial, but is primarily due to the fact that in most European countries, while the system for organ donation for transplantation is well established, there are no clearly defined guidelines on the distribution of non-transplantable human tissue for research. The major consequence of a lack of guidelines is that health professionals, in particular, are wary of procuring tissue for research, because there might be ethical and legal implications of which they are not aware. Even when health professionals do wish to be involved in facilitating research by procuring non-transplantable cadaveric tissue.

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1The term research is used in a generic sense to cover fundamental and applied experimental work and testing.
use of the tissue. Consequently, the donation of non-transplantable organs for research generally tends to be carried out on an ad hoc basis through collaborative arrangements between individual scientists and surgeons. The amenability and the location of surgeons and scientists restrict the availability of human tissue through such a route, so this kind of arrangement is generally restricted to collaborations between researchers and surgeons working within the same hospital. Furthermore, these collaborations can also raise some important ethical and safety issues.

A substantial proportion of the general public refuse to donate tissue for transplantation (5, 6), and there has been concern that, if potential donors or their families felt that their donation would be used for research, this could adversely affect the number of people willing to donate for transplantation. Although there are reports that suggest that these fears are unfounded (7), it is imperative that in all strategies and legislation for facilitating the availability and use of human tissue for research, it is recognised that the needs of tissue and organ transplantation programmes, and pathological examinations of tissue, must take priority. It is also important to reassure the public that the donation of tissue for research does not adversely affect the organ transplantation programme, and information should be provided for health workers and the general public to explain the benefits of using human tissue for research.

Ideally, human tissue would be readily available for suitably accredited scientists to use for socially beneficial and scientifically important purposes. However, in Europe, the demand for human tissue by scientists in both industry and academia is currently greater than the supply. Furthermore, it is likely that the limited availability of human tissue is contributing to delays in the acceptance by regulatory authorities of in vitro methods to replace in vivo experiments in animals.

The tissue banks that have been established throughout Europe usually only provide tissue for transplantation and not for research. Consequently, for several years, researchers in Europe have imported human tissue from the USA from non-profit making distributors such as the International Institute for the Advancement of Medicine (IIAM), the Association of Human Tissue Users and the National Disease Interchange. The disadvantages of transporting human tissues over long distances include the high costs involved and problems with tissue preservation. In 1996, the IIAM in the UK was established as the first tissue bank in Europe dedicated to the distribution of human tissue for research. More recently, the UK Human Tissue Bank was launched with the objective of improving the regularity with which tissue can be procured and distributed by employing a transplant coordinator solely to procure tissue for research. There are also initiatives to establish research tissue banks in The Netherlands and Belgium.

This workshop addressed a variety of issues related to improving the availability of human tissue throughout Europe, in an attempt to build upon the findings of previous reports (6, 8) and symposia (4, 9, 10). These issues include: a) ethical and legal issues; b) safety issues; c) logistics; and d) end-user requirements.

**Ethical and Legal Issues**

In an attempt to improve the system of organ donation for transplantation, European countries have adopted various legal frameworks. Countries have either an “opting in” system, whereby potential donors must register their wish to be organ donors, or an “opting out” system, in which it is presumed that people give their consent unless they register their objection. In the former case, relatives are also required to give their consent in the event of the donor’s death, while in the latter case, it is not necessary to inform relatives before the removal of tissues, although in practice this often happens. The various strategies for the donation of human tissue in the European countries represented at this workshop are presented in Table I.

The legal framework in European countries for the donation of non-transplantable human tissue for research is rather unclear. For example, in France, the law governing the use of cadaveric tissue for research is not defined; in general, such tissue is only used to facilitate research associated with transplantation. However, in several other European countries, ethically approved research
can involve the use of surplus surgical and cadaveric tissue. A lack of guidelines can dissuade surgeons and transplant coordinators from becoming involved in the procurement of tissue for research. For the donation of non-transplantable cadaveric or live donor human tissue for research, either an “opting in” or an “opting out” system could be adopted, but the principle of consent is important in both cases.

It is the responsibility of a surgeon to obtain consent from a living donor for the use of sur-

Table I: Current status of the process of human tissue donation in the European countries represented at the workshop

<table>
<thead>
<tr>
<th>Country</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>Opt-out system. No informed consent is needed for surplus surgical tissue to be used for research, but consent is required for all the safety tests that need to be conducted on the tissue before it can be used. Any waste following the use of the tissue for research must be collected by an authorised company for safe disposal. A new law permits only listed or accredited laboratories to collect, process, sell or use surplus surgical tissue. The situation regarding the use of cadaveric tissue for research is unclear.</td>
</tr>
<tr>
<td>UK</td>
<td>Opt-in system. A donor card obviates the need to ask relatives for their lack of objection for cadaveric tissue to be used for transplantation. However, in practice, relatives’ lack of objection is always sought. If tissues are not suitable for transplantation, relatives can be asked if they are willing for tissues to be used for research (The Human Tissue Act 1961). There is some ambiguity surrounding the legality of using surplus surgical tissue for research. Under UK law, tissue that would be thrown away is considered “abandoned” and as such, it can be used for research considered to be in the public interest (23).</td>
</tr>
<tr>
<td>Belgium</td>
<td>Opt-out system. Principle of non-commercialism. No consent is required for using cadaveric material, but is required for living donors (although this is not strictly adhered to). HIV testing is possible without a patient’s consent. Legislation is limited to the use of human tissues for therapeutic purposes.</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Opt-in system. Passing the tissue on to a third party is not allowed. No specific consent is required for transplantation-related research using cadaveric or surplus surgical tissue. There are two possibilities for surplus surgical tissue to be used for other types of research — either the tissue can be used anonymously without consent and the patient receives limited information, but has the right to object to the tissue being used for research, or the patient details are recorded, and the patient receives extensive information and has to give consent for the tissue to be used for research.</td>
</tr>
<tr>
<td>Germany</td>
<td>Opt-in system. Commercialism for transplant tissue. Situation for non-transplantable tissues is unclear.</td>
</tr>
</tbody>
</table>
plus surgical tissue for research, and the responsibility of a transplant coordinator to obtain consent from the next of kin of a cadaveric donor. Obtaining consent can be an extremely sensitive issue, and giving the living donor or donor’s next of kin detailed and extensive information about the end-use of the tissue to be donated could be overwhelming at a difficult time. Instead, “general”, rather than “specific” consent should be obtained. General consent should cover the end user and the hospital from an ethical and a legal point of view. In the case of living donors, general consent could be obtained by the addition of a simple statement to the general consent form for surgical/anaesthetic procedures. An example of a consent form that has been used successfully is shown in Figure 1. The addition of a short statement to an existing form obviates the need for separate consent forms, and makes the consent procedure less time-consuming for health professionals.

Figure 1: A standard consent form for anaesthetic and surgical procedures, modified to include consent for non-transplantable tissues to be used for research

<table>
<thead>
<tr>
<th>I am the patient/parent/guardian (delete as necessary).</th>
</tr>
</thead>
<tbody>
<tr>
<td>I AGREE to the proposed treatment which has been explained to me by the doctor/dentist on this form.</td>
</tr>
<tr>
<td>to the use of the type of anaesthetic that I have been told about (if applicable).</td>
</tr>
<tr>
<td>to the use of any tissue necessarily removed during this operation to be used for research.</td>
</tr>
<tr>
<td>I UNDERSTAND that the procedure may not be done by the doctor/dentist who has been treating me so far.</td>
</tr>
<tr>
<td>that any procedure in addition to the investigation or treatment described on this form will only be carried out if it is necessary and in my best interests and can be justified for medical reasons.</td>
</tr>
<tr>
<td>I HAVE BEEN ADVISED by the doctor/dentist about additional procedures which may rise.</td>
</tr>
<tr>
<td>I have detailed below which of these I do not wish to be carried out without further consultation and consent.</td>
</tr>
</tbody>
</table>

Signature .................................................................
Name .................................................................
Address .................................................................
It is important that donors, and donors’ relatives in the case of cadaveric donations, have available to them a clear explanation of what is meant by the term "medical research". Additional information specific to the research for which the tissue is going to be used should be made available to donors or donors’ relatives upon request. This information can be important in reassuring health professionals, donors, and donors’ relatives that the tissue is being used to support the type of research of which they would approve.

A positive response from a donor or a donor’s next of kin to a request for consent to use non-transplantable organs for research should be considered an act of altruism. As such, the donor or donor’s next of kin should have no legal right to the donated tissue after its removal. The principle of altruism should also extend to anyone involved in the procurement and supply of human tissue, to ensure that rewarded gifting does not take place.

From an ethical and a legal point of view, it is highly desirable to establish tissue banks across Europe as non-profit making repositories for human tissue for research, whereby safety and accountability can be guaranteed. The tissue banks should act as custodians of human tissue, involved in both its procurement and its distribution to accredited end-users (Figures 2 and 3; 11). While it is illegal in Europe for human tissue to be bought or sold, the cost of procurement and transport of the tissue could justifiably be recovered, provided that the organisation remains non-profitable. Any funds accrued above those required to operate the tissue bank should be used to further the aims and objectives of the tissue bank.

Transparency and probity must extend from the initial contact that is made with the donor or the donor’s next of kin, through the operational procedures of the tissue bank, to the end-user. End-users should be aware of the whole process involved in the procurement of cadaveric and surgical tissue for research purposes.

End-users should be subject to a form of accreditation so that a minimum set of criteria are fulfilled before tissue is distributed. Such criteria should include an assurance that the establishment wishing to conduct the research has the appropriate facilities and knowledge to ensure optimum use of the tissue and to permit the safe handling and disposal of human tissue. Each establishment should also be shown to have ethical and scientific credibility. Accreditation could be awarded by an independent review panel. Such a panel could include scientists and medical experts reporting independently and directly to the research tissue bank.

Tissue banks should use a secure tissue management system, to ensure that fully anonymised information is maintained and that donations are traceable. In this way, all health professionals involved in the donation procedure, and the relevant governmental departments, can be provided with evidence that the confidentiality of the donor, the donating hospital and health workers is being fully protected.

Safety Issues
A primary consideration in the research use of human tissues is the safety of all the personnel who will be, or could be, exposed to such tissues, or any product obtained from them, such as cell cultures or cell fractions. The most important aspects of ensuring safety are awareness, suitable handling procedures and the provision of adequate training of all users. Significant viral pathogens that could be encountered include Hepatitis B, Hepatitis C, HIV and cytomegalovirus (CMV) all of which have specific known pathogenicities, and the recently identified HHV8 (Kaposi’s sarcoma virus), which may cause tumours under certain circumstances. In addition, the possibility of bacterial hazards, such as Mycobacterium sp., and antibiotic resistant organisms, such as methicillin-resistant Staphylococcus aureus, should not be ignored, as these are becoming increasingly frequent among hospital cases.

While it is possible to test for a number of viral and bacterial pathogens, there are significant residual risks even when this testing has been done. Therefore, such testing does not absolve either the provider of non-transplantable tissue or the end-user from taking appropriate precautions against known and unknown hazards (12, 13). As the cases of HHV8 and Kaposi’s sarcoma, and Coxackie-4 and juvenile diabetes have recently demonstrated, new human viruses with pathogenic connotations have been discovered at least
Figure 2: A schematic diagram showing how tissue banks could act as intermediaries in order to facilitate the availability of surplus surgical tissue for research.

1. Consultant surgeon and colleagues agree to support specific kinds of biomedical research.
2. Consultant surgeon in charge of case obtains patient’s consent to proceed with the operation and use of surplus tissue for research.
3. If permission is not granted, surplus tissue is incinerated.
4. Research tissue bank staff are informed by consultant surgeon.
5. Research tissue bank staff attend theatre to collect surplus tissue.
6. Tissue taken back to research tissue bank.
7. Distribution to accredited biomedical researchers.
8. Feedback given with regard to use of donated tissue.
Figure 3: A schematic diagram showing how tissue banks could act as intermediaries in order to facilitate the availability of non-transplantable cadaveric tissue for research.

1. Intensive care unit staff
2. Patient in hospital intensive care unit
3. Diagnosis of brain stem death
4. Transplant coordinator involvement
5. Consent sought from relatives for organs and tissues for transplantation
6. Consent sought from relatives for non-transplantable organs/tissues for research use
7. Research tissue bank staff notified and non-transplantable material collected via ambulance courier or tissue bank staff
8. Distribution to accredited biomedical researchers
9. Feedback given with regard to specific use of donated tissue
every 5–10 years, and more are likely to follow in the future. Thus, whatever the results of specific testing, all human tissue must be considered to be hazardous at all stages of its experimental use and disposal.

The safe use of human tissue that might contain known and unknown infectious agents depends on:

1. secure containment during collection, transport and use, which minimises exposure of laboratory personnel and transportation couriers directly handling such tissues;
2. effective methods of sample decontamination prior to release for disposal from the laboratory, to eliminate risk to the environment and “passers-by”; and
3. strict protocols for the handling and disposal of human tissue waste.

The number of people directly exposed to such risks should be kept to an absolute minimum and strictly limited to those who have sufficient knowledge and training to be considered “informed” as to their personal risk. All such personnel should be provided with whatever effective and safe immunisations are available at the time.

Although maximum risk is usually associated with fresh tissue samples due to their freshness, bulk and blood content, this is not always the case. Specific laboratory procedures may actually increase, rather than decrease, risk in certain instances. Tracking methods that clearly identify samples of human tissue origin, especially when this is not obvious by inspection, for example, tissue homogenates or DNA extracts (which may contain viral DNA), are essential, to ensure that the appropriate containment is maintained at all times up to and including the final disposal and decontamination of all samples. Specific procedures that may amplify a hazard and thus greatly increase risk, such as the in vitro culture of a susceptible cell type from a potentially infected donor, must be clearly identified, and the risks posed should be separately assessed before proceeding with such experiments.

**Logistics**

The logistics of getting human tissue from the location of its procurement to an end-user is an important consideration when attempting to improve the availability of human tissue for research. The establishment of a Europe-wide network of tissue banks could increase the efficiency with which human tissue is procured and distributed to end-users. Such a network should be able to provide a 24-hour, 7 day per week service that can quickly respond to notification of the availability of non-transplantable human tissue in situations where particular end-users would not be able to make themselves available.

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human tissue before it is used. Research of this kind would allow the formulation of standardised procedures for the preservation and transport of tissues within a country and between countries.

Human tissue should be transported in standardised, clearly labelled containers by tissue bank staff, by a courier service dedicated to the transport of human tissue, or by a general courier service specifically informed about the nature of the material and the requirements for its transportation.

It is essential that tissue bank staff establish a good relationship with transplant coordinators and surgeons able to procure non-transplantable tissues for research. The willingness of these health professionals to donate their time and expertise to procuring tissue for research depends in part upon them receiving adequate information from end-users, tissue banks and the medical literature about the benefits of using human tissue both for research and for society as a whole. In addition, health professionals who have procured tissue for research should receive feedback from the end-user, via the tissue bank, about the progress of the research for which the tissue has been used.

The tissue bank should ensure that health professionals are aware of the working practices in operation within the tissue bank facility. This could be achieved through meetings both within hospitals and at the tissue banks, where an opportunity could be provided for any concerns to be raised about aspects of procuring tissue for research purposes. Such concerns might include patient and hospital confidentiality and the types of research for which the tissue would be used.

End-users can, on occasion, find themselves in possession of tissue that is surplus to their requirements and which it is not possible to store. This tissue is often disposed of, because the end-user is not aware of other researchers who might benefit from receiving it. A useful role of tissue banks would be for them to act as intermediaries able to advise an end-user of any researchers known to be in need of such tissue.

The Requirements of the End-user

The potential uses of human tissue are extensive, but they can be broadly divided into three categories: teaching and training; basic research; and safety and efficacy testing.

Human tissue can be used as tissue slices that allow the study of cells maintained in their natural matrix in vitro (16). Human cells isolated from tissues can be used to produce cell lines or to produce reconstructed tissue models. Reconstructed tissue models have been developed with hepatocytes (17), corneal cells (18) and keratinocytes (19), and some models are commercially available. Researchers also require subcellular fractions such as microsomes.

Human tissue is currently being used during certain safety testing procedures that are conducted by or for industry in order to protect human health (Table II). Unlike animal tissue, fresh human tissue can exhibit the full range of specifically human target enzymes that are essential for pharmacokinetic and metabolism studies conducted during the development of new drugs, industrial chemicals and food additives (20).

In addition to healthy tissue, diseased tissue is also required for use in studies of human diseases, and to assist in the development of new therapies.

Increasing the availability of human tissue is only one aspect of facilitating the use of human tissue in research. The establishment of a network of tissue banks would be futile, if they were only able to increase the regularity and reliability of supply to end-users; steps must also be taken to ensure that tissue is delivered in a satisfactory condition.

Tissue banks could deal with specific requirements that are regularly requested; for example, during procurement and preservation of tissues, some researchers require perfusion and transport on ice, while others request that tissues are snap frozen or cryopreserved.

Some requests from end-users are for isolated cells; for example, isolated hepatocytes for use in metabolism studies prior to toxicity testing of chemical agents. Isolation procedures can adversely affect the normal physiological state of the cells. More research is necessary into isolation techniques, so that standardised procedures that minimise damage can be produced. For the scientifically valid use of human hepatocytes, it will be necessary to characterise the cells to ensure their viability and function has not been impaired by their isolation.
Table II: Examples of uses of human tissue for efficacy, mechanistic and safety testing

<table>
<thead>
<tr>
<th>Stage of safety testing</th>
<th>Studies conducted</th>
<th>Types of human tissue required</th>
<th>Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discovery</td>
<td>For the prediction of efficacy. For example, receptor binding assays and enzyme inhibition.</td>
<td>Any target organ</td>
<td>Pharmaceutical</td>
</tr>
<tr>
<td></td>
<td>For the prediction of safety, cytotoxicity studies are used for the early identification of intrinsic toxicity potential prior to regulatory toxicity testing.</td>
<td>Priorities include corneal, cardiovascular reproductive, respiratory, renal</td>
<td>Pharmaceutical, chemical, agrochemical, cosmetic, food</td>
</tr>
<tr>
<td></td>
<td>Metabolism and pharmacokinetic studies.</td>
<td>Microsomes</td>
<td>Pharmaceutical</td>
</tr>
<tr>
<td>Development</td>
<td>Metabolism and pharmacokinetic studies to compare effects of a test agent in human cells with animal cells in order to identify the most suitable agents for further development and the most appropriate species for subsequent in vivo toxicity tests. The only regulatory test requiring the use of human tissue is for qualitative assessment of drug-drug interactions using human microsomes during metabolism studies.</td>
<td>Hepatocytes/microsomes</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>Human tissues can be used to study mechanisms of toxicity to investigate the relevance of animal responses to humans. These mechanistic studies can be used to accompany regulatory studies.</td>
<td>All</td>
<td>Pharmaceutical, chemical, agrochemical, cosmetic, food</td>
</tr>
<tr>
<td></td>
<td>Studies for percutaneous absorption, inflammation, corrosivity and sensitisation. Some systems have undergone or are undergoing validation, but have not yet gained regulatory acceptance.</td>
<td>Corneal, skin</td>
<td>Cosmetic</td>
</tr>
</tbody>
</table>
The administration of certain drugs to a patient prior to tissue donation for research could affect the suitability of the tissue for use in both fundamental research and in safety testing procedures. Therefore, it should be possible for requests for clinical drug records from donor hospitals to be specified by the end-user, where appropriate.

Where end-users have very specific or varied needs that would be difficult for a tissue bank to meet, collaboration between end-users and surgeons will continue to be the most effective method of obtaining tissue. Collaboration of this kind is often necessary when end-users require tissue immediately after its procurement. When tissue is distributed via such routes, it is essential that the tissue supply has been documented, and that its end-use has been ethically approved.

Tissue banks and end-users would benefit from a knowledge exchange system whereby tissue bank staff could learn specific techniques for isolation and preservation from the end-user, and the end-user could visit the tissue bank to see how the tissue was processed before distribution.

The viability and usefulness of tissue and cells distributed to end-users depends on the preservation methods used (21) and on how quickly the tissues can be transported to their destination. Research is necessary to establish the most suitable transport conditions for a range of cell and tissue types. For human hepatocytes, for example, it might be advantageous to transport the cells in culture or as tissue slices (22).

Conclusions

General

1. Human tissues should be regarded as a precious resource, to be used with careful consideration and with respect.

Legal and ethical issues

2. The fundamental principle of obtaining consent should be based on a general, rather than a specific, willingness, and can be achieved by the potential donor actively agreeing (opting-in) or not actively disagreeing (opting-out) to donate tissue.

3. A positive response to a request for consent to use human tissue for research by a donor or a donor’s next of kin should be considered to be an act of altruism. The principle of altruism should extend to ensuring that rewarded gifting does not take place at any stage.

4. While not inhibiting collaborations between researchers and surgeons and/or pathologists, tissue banks should be considered to be the preferred method of dealing with the procurement and distribution of human tissue.

5. Education about the value of using human tissue for research purposes should be targeted at the general public and also at surgeons and transplant coordinators. This could be achieved by preparing general articles for publication in the medical, scientific and general literature, on the establishment and role of tissue banks and on the general requirement for a wide variety of human tissues for research.

Safety issues

6. Human tissue should be treated as biohazardous material and should only be handled by adequately protected and properly trained personnel.

7. The dissemination of information regarding national and international transport and packaging regulations and the use of dedicated couriers would facilitate the distribution of human tissue.

8. To avoid cross-contamination in laboratories, which might compromise safety, dedicated laminar flow cabinets should be used for the handling of human tissues whenever possible, ideally located in rooms with restricted access.

Logistics

9. The ideal method of facilitating the efficient procurement and distribution of human tissues to end-users would be the establishment of a network of registered tissue banks providing a communication link between health professionals and users.

10. There needs to be continuous feedback and dialogue among surgeons, transplant coordinators, other health professionals, tissue banks and end-users.
regarding all aspects of the procurement, processing and use of human tissues, and, in particular, any scientific advances achieved as a result of the use of such material.

The requirements of the end-user

11. The availability of scarce human tissues for special purposes, such as diseased tissue for research, should be improved as a means of facilitating the development of treatments for diseases.

12. There is a need for representative panels of permanent human cell lines with stable tissue-specific properties, to reduce the need for freshly isolated tissue. This will require identification of the current status of the technology for producing such cell lines and the principal limitations on progress, in addition to continued research to improve the technology.

Recommendations

General

1. Governments and legislators should be kept fully informed about the important contributions to healthcare that the use of human tissue for research purposes can make, as well as contributing to the replacement of animal experiments.

2. Where necessary, changes to the legal frameworks operating in European countries should be sought in conjunction with the relevant authorities, in order to facilitate the procurement of surgically removed human material surplus to medical requirements, and its supply in a suitable form to end-users.

Legal and ethical issues

3. The consent form used by Queen Mary’s Hospital, Roehampton, UK (Figure 1), is recommended as a suitable example for obtaining general consent from living donors for the provision of human tissue for research.

4. The use of tissue banks should be recognised as the most legally and ethically acceptable approach to the procurement and distribution of donated non-transplantable human tissue for research.

5. A tissue-tracking system should be established to guarantee the anonymity of the donor, the donor’s family and health professionals involved in a donation. This should also involve routes of communication between the researcher and the surgeon, via the tissue bank that originally supplied the tissue in question, when appropriate.

6. Users of human tissue should undergo a process of accreditation, to ensure that a minimum set of criteria are fulfilled. These criteria will include safety issues, scientific reputation, ethical credibility, proper training, suitable facilities for safe handling and disposal of human tissue, and confidentiality. Wherever possible, this accreditation should be conducted via an appropriately qualified and independent expert group.

7. Informative articles on the establishment and role of tissue banks, and on the need for a wide variety of human tissue for research, for publication in the medical, scientific and general literature, should be prepared by those interested and involved in this area of work.

8. The availability for research purposes of human tissue, surplus to medical requirements, should be facilitated by all available means; for example, by distributing newsletters, short articles and instructional videos, to improve communication between end-users and health professionals.

Safety issues

9. All human tissue should be regarded as potentially biohazardous and should be handled accordingly by appropriately trained personnel. Specific and appropriate precautions should be taken against known hazards, and general precautions against unknown hazards.

10. Tissue banks should ensure that human tissues have been screened for specific biohazards, where possible and as appropriate. Such information should be made available to the end-user as quickly as possible. Ideally, this should be before any exposure of the end-user to the tissue. It is recognised, however, that this might not always be possible. Safety information should be used to
modify any risk assessment already undertaken, with subsequent adjustment of handling procedures, or immediate disposal of the material, as appropriate.

11. All those potentially exposed to human tissue should be vaccinated against hepatitis B virus, and should be shown to exhibit the nationally accepted level of immunisation before any possible exposure; they should also be regularly checked for level of immunity.

12. All human material, and disposable equipment used in conjunction with human tissue, should be sterilised according to a recommended procedure before transport for incineration.

13. All research facilities involved in the use of human tissue should have relevant, standard protocols for ensuring its safe handling and disposal. Guidelines to be used as a basis for these protocols should be made available.

14. Safety courses should include information specific to the handling of human tissue.

15. Organisations such as the European Association of Tissue Banks, which has devised training courses for the safe handling of human material for transplantation, should be encouraged to make similar courses available to providers and users of non-transplantable human tissue.

16. The nature and content of such courses, and records of staff attendance, should be documented, and maintained within the relevant establishments.

17. There should be standardisation of containers and labelling with respect to the movement of surgical and non-transplantable human tissue for research, so that they are easily recognisable.

18. Information regarding regulations for packaging and national and international transport of human tissue should be collated into a database and made generally available.

Logistics

19. Tissue banks should establish procedures for providing advice to end-users who find themselves with human tissue surplus to their requirements which could be useful to other end-users.

20. Tissue banks and others, including end-users, should undertake research which will enable, as far as possible, the regular and reliable supply of cells from all human tissue of sufficiently high quality for research. Issues requiring further research include isolation, preservation and storage techniques, and suitable conditions for distribution.

Requirements of the end-user

21. Tissue banks should be transparent about the procedures involved in the isolation, storage and sterilisation of human tissue. This would be facilitated if staff at tissue banks and end-users visited each other’s establishments to view techniques and procedures.

22. A list of suitable quality control criteria for each type of tissue and use should be drawn up by tissue banks, in conjunction with end-users. This is particularly important where a use is for regulatory purposes, when specific criteria will have to be met to satisfy a particular regulatory guideline. Flexibility in structural and performance criteria for using human tissue for regulatory purposes should be increased where this is possible without compromising scientific output, by dialogue among tissue banks, end-users and regulatory bodies.

23. Attempts should be made to satisfy end-user requirements by standardising the preparation and quality of specific cell types, and standardising the transport conditions for their distribution.

References

