Organs, Tissues and Cells

Safety, Quality and Ethical Matters Concerning Procurement, Storage and Transplantation

Council of Europe Resolutions, Recommendations and Reports

1st Edition
Organs, Tissues and Cells – Safety, Quality and Ethical Matters Concerning Procurement, Storage and Transplantation

Council of Europe resolutions, recommendations and reports
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Recommendations
The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the health field;

Taking account of the ethical principles set out in Recommendation No. R (88) 4 on responsibilities of health authorities in the field of blood transfusion concerning voluntary, non-remunerated blood donation;

Considering that, in the procurement and distribution of human tissues, the ethical principles concerning organ transplantation as set out in Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of
human substances, and agreed at the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987), should be respected under all circumstances and that consent is required for the removal of tissues and their proposed use, whether therapeutic, diagnostic or research;

Taking account of World Health Organisation Resolution WHA 42.5 condemning the purchase and sale of organs of human origin;

Noting the fact that human tissue is donated by the public for altruistic reasons;

Taking note also of the questions of interpretation provided for in the appendix to this recommendation,

Recommends to the governments of member states:

1. That activities related to the banking of human tissue be divided into the following separate functions, it being understood that such functions in no case extend to the collection of such tissue:
   - organisation;
   - processing;
   - preservation;
   - internal quality control;
   - storage;
   - distribution;

2. That these functions be carried out by non profit-making institutions which are officially licensed by national health administrations, or recognised by the competent authorities;

3. That, by way of derogation from paragraph 2, in the case of a public health need, the activities described in paragraph 1 may be carried out by a duly authorised profit-making body;

4. That tissue banks ensure that tissue be tested for transmittable diseases, in compliance with the law and practice of the country concerned;
5. That tissue banks store the tissue safely according to scientifically recognised state-of-the-art techniques and respecting the criteria established by general medical and laboratory practice;

6. That records of all tissues retrieved and issued be kept by the tissue banking organisations in such a way that their source and their destination are clearly identifiable, providing always that access to such records will be restricted to the extent necessary to protect confidentiality of information and individual privacy;

7. That distribution take place in such a way as to permit optimal use of the tissues on an equitable basis in accordance with national law, rules and practice and objective selection criteria;

8. That close mutual co-operation be pursued by all officially recognised exchange and tissue banking organisations and that follow-up data on donor/recipient combinations should be shared between relevant institutions within the framework of national guidelines and legislation providing always that the privacy of the person concerned is fully respected.

Appendix to Recommendation No. R (94) 1

Definition of human tissue (for example skin, bone and cornea)

For the purposes of this recommendation, human tissue includes all constituent parts of the human body, including surgical residues but excluding organs, blood and blood products as well as reproductive tissue, such as sperm, eggs and embryos. Hair, nails, placentas and body waste products are also excluded.
Council of Europe
Committee of Ministers

Recommendation No. R (97) 15 of the Committee of Ministers to member states on xenotransplantation

(Adopted by the Committee of Ministers on 30 September 1997 at the 602nd meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the health field;

Taking into account Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987) and Articles 19 and 20 of the Convention on Human Rights and Biomedicine;

Considering that xenotransplantation, that is, the use of living organs, tissues and/or cells from animals, whether genetically modified or not, for transplantation into humans, may become a practicable therapeutic intervention in the very near future;
Aware that there is a risk of transmission of disease as a result of xenotransplantation procedures,

Recommends that governments of member states should, with a view to minimising the risk of transmission of known or unknown diseases and infections to either the human or animal populations, establish a mechanism for the registration and regulation of the following aspects of xenotransplantation:

i. basic research and clinical trials;
ii. the source and care of animals for use in xenotransplantation;
iii. xenotransplantation programmes;
iv. long term follow-up and review of xenograft recipients and the xenograft source animals.
The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the health field;

Considering that liver donations by living related donors saves the lives of children;

Bearing in mind that, in liver transplantation with living related donors, the ethical principles concerning organ transplantation as set out in Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, and agreed at the 3rd Conference of European
Recommendations of the Committee of Ministers to member states

Health Ministers (Paris, 16-17 November 1987), should be respected under all circumstances and that fully informed consent is required from both the donor and the recipient;

Mindful of the provisions of Articles 19, 20 and 21 of the Convention on Human Rights and Biomedicine;

Taking account of World Health Organisation Resolution WHA 42.5 condemning the purchase and sale of organs of human origin,

Recommends that governments of member states conform to the rules set out in the appendix to this recommendation in carrying out living related liver transplantation (LRLT).

Appendix to Recommendation No. R (97) 16

1. LRLT should be considered only when there is a shortage of cadaver organs, that is when alternatives that do not carry the risks incurred by a living donor have been exhausted.

On the evidence currently available, LRLT should be considered only for children and should not be recommended for adults nor in an emergency situation such as fulminant liver failure.

2. Potential recipients of LRLT should have been previously assessed as suitable for cadaveric transplant and, if considered suitable for LRLT, should still be retained on the waiting list for the cadaveric programme in case a suitable liver becomes available. If it is unlikely that a suitable cadaveric liver will become available within the required timescale, then the patient and relatives should be informed of the possibility of LRLT.

3. The potential risks, including morbidity and mortality, arising from LRLT as well as its benefits should be explained to the potential recipient. The consent of the donor should be
obtained only after a full explanation of the risks of LRLT and an assessment of the donor’s suitability by a third party, that is a “donor advocate” independent of the transplant team.

Fully informed consent should also be obtained from the recipient (or recipient’s representative).

iv. Minors and adults not having the capacity to consent to an intervention because of a mental disability, a disease or for similar reasons should not be considered as donors.

v. Centres performing LRLT should have available a body of medical and non-medical professionals independent of the team performing the transplant to provide guidance on ethical issues relating to LRLT. A mechanism for independent assessment of the donor should be available as a minimum requirement to ensure that he/she is not under pressure to consent.

vi. LRLT should be performed only in centres with extensive experience of all aspects of liver surgery, notably liver splitting techniques, and adult and paediatric liver transplantation, and within the framework of a quality assurance programme.

Centres should perform LRLT procedures only with the approval of an appropriate transplant regulatory body.

The procedures should be registered with the regulatory authority and the results monitored by a recognised method of peer review (until the results are considered acceptable).

vii. Living related donors should not participate in medical experiments unless their objective is to evaluate the LRLT.
The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the health field;

Taking account of the ethical principles set out in Recommendation No. R (88) 4 on responsibilities of health authorities in the field of blood transfusion concerning voluntary, non-remunerated blood donation;

Taking account of the ethical principles set out in Recommendation No. R (94) 1 on human tissue banks;

Recalling its Recommendation No. R (95) 14 on the protection of the health of donors and recipients in the area of blood transfusion;
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Recalling the guidelines and principles defined in Recommendation No. R (95) 15 on the preparation, use and quality assurance of blood components;

Recalling also its Recommendation No. R (97) 5 on the protection of medical data;

Considering that, in the procurement and distribution of haematopoietic progenitor cells, the ethical principles concerning organ transplantation as set out in Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, and confirmed at the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987), should be respected under all circumstances and that consent is required for the removal of tissues and their proposed use, whether therapeutic, diagnostic or research;

Taking account of World Health Organisation Resolution WHA 42.5 condemning the purchase and sale of organs of human origin;

Taking note of the definition provided for in the appendix to this recommendation;

Bearing in mind the Convention on Human Rights and Biomedicine as well as Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data,

Recommends to the governments of member states the principles set out in the appendix to this recommendation.

Appendix to Recommendation No. R (98) 2

1. The activities relating to the provision of haematopoietic progenitor cells can be divided into the following separate functions:
   - donor selection;
   - organisation;
Recommendations of the Committee of Ministers to member states

- collection;
- processing;
- preservation;
- internal quality control;
- storage and release /issue from storage;
- distribution;
- quality assurance and good laboratory practice (GLP).

2. The functions described under paragraph 1 should be carried out by institutions which are officially licensed by national health administrations, or recognised by the competent authorities. These institutions should not make any gain from their activities as such.

3. The organisations involved in haematopoietic progenitor cells should ensure that donors of haematopoietic progenitor cells be tested for transmittable diseases, in compliance with the law and practice of the country concerned.

4. The organisations involved in work on haematopoietic progenitor cells should implement scientifically recognised state-of-the-art techniques (such as CD34 positive cell numbers, cell viability and sterility) and respect the criteria established by general medical and laboratory practice, and implement an effective quality assurance system (such as GLP).

5. Records of all haematopoietic progenitor cells retrieved and issued should be kept by the organisations involved in haematopoietic progenitor cell transplantation in such a way that their source and their destination are clearly identifiable, providing always that access to such records will be restricted to the extent necessary to protect confidentiality of information and individual privacy; donors and recipients should be followed up for at least twenty years.

6. Criteria for the collection of haematopoietic progenitor cells should be established in accordance with national law. Distribution should take place in such a way as to permit optimal use of haematopoietic
Recommendations of the Committee of Ministers to member states

progenitor cells on an equitable basis in accordance with national law, rules and practice and objective selection criteria. Cells for transplantation should be released only to those centres which according to national law are qualified to perform autologous or allogenic progenitor cell transplantations.

7. Close mutual co-operation between different professional groups such as those working in bone marrow transplantation and blood banks should be pursued by all officially recognised organisations concerned with activities involving haematopoietic progenitor cells, and follow-up data on donor/recipient combinations should be shared between relevant institutions within the framework of national guidelines and legislation, provided always that the privacy of the person concerned is fully respected.

8. Close mutual co-operation between different professional groups such as those working in bone marrow transplantation and blood banks should be pursued by all officially recognised organisations concerned with activities involving haematopoietic progenitor cells with the aim of agreeing common minimum quality standards for haematopoietic progenitor cells and the procedures for handling haematopoietic progenitor cells outlined under paragraph 1.

9. All family and unrelated donors of haematopoietic progenitor cells, and the mothers of infants donating cord blood, are to be given appropriate information on known risks about the methods of donation, from a physician who is independent of the Bone Marrow Transplant team. Mothers of infants donating cord blood must give their consent prior to collection which must be non-remunerated.

10. Cord blood banks should observe ethical standards and such banks should achieve the standards recommended under paragraph 5 from their inception.

Definition of haematopoietic progenitor cells

11. For the purposes of this recommendation, haematopoietic progenitor cells (HPC) are primitive pluripotent cells capable of self renewal as well as differentiation and maturation into all
haematopoietic lineages. They are found in bone marrow, foetal liver, in the mononuclear cells of circulating blood and in umbilical cord blood.

12. Haematopoietic progenitor cell preparations (from all four sources) are intended to provide a successful engraftment of haematopoietic stem cells leading to a restoration of all types of blood cells to a normal level and function in the recipient. The infused haematopoietic cells may originate from the recipient or from another individual.
Council of Europe
Committee of Ministers

Recommendation Rec(2001)5 of the Committee of Ministers to member states on the management of organ transplant waiting lists and waiting times

(Adopted by the Committee of Ministers on 7 March 2001 at the 744th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the public health field;

Bearing in mind Article 11 of the European Social Charter on the right to the protection of health;

Recalling that Article 3 of the Convention on Human Rights and Biomedicine requires that Contracting Parties provide “equitable access to health care of appropriate quality”;
Recommendations of the Committee of Ministers to member states

Taking into account Resolution (78) 29 on the harmonisation of legislations of member states relating to removal, grafting and transplantation of human substances, the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987) and Articles 19 and 20 of the Convention on Human Rights and Biomedicine;

Having regard to Recommendation No. R (99) 21 on criteria for the management of waiting lists and waiting times in health care;

Considering that the collection of medical data raises special concerns with regard to data protection, especially where the data are to be collected or used for purposes other than immediate health benefits to the individual;

Having regard to the Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data (ETS No. 108) and to Recommendation No. R (97) 5 on the protection of medical data;

Aware that waiting lists and waiting times may appear when the demand for organs exceeds availability;

Taking account of World Health Organisation Resolution WHA 42.5 condemning the purchase and sale of organs of human origin;

Considering that organ transplantation is severely restricted by the availability of organs for transplantation and that a properly managed waiting list is essential to ensure equality of access to organ transplantation,

Recommends that governments of member states conform to the following rules:

1. Member states should guarantee that a system exists to provide equitable access to transplantation services for patients which ensures that organs and tissues are allocated in conformity with transparent and duly justifiable rules according to medical criteria.

2. There should be a mechanism, enforceable by law or regulations, for establishing and managing an officially recognised regional, national or international waiting list for each of the main types of organ transplantation.
3. Cadaveric organs should only be allocated to patients registered on the official waiting list. Patients receiving organs from a living donor should also be registered if there is any possibility that they might need an organ from a deceased person.

4. Patients may only be registered on one official transplant waiting list be it regional, national or international. Individual transplant units may have their own local waiting list but only as a subset of the official waiting list.

5. Criteria for registration on the waiting list should be established by a process of consensus based on medical criteria. Registration should include the data essential to identify patients individually, their location and the criteria for their inclusion on the waiting list. The criteria for inclusion should ensure there is no discrimination on the grounds of race, religion, disability or any other non-medical factor. Priority on the waiting list such as “urgent” or “very-urgent” categories should be based solely on medical factors relating to the severity of risk for the individual patient. If patients are registered who do not normally reside in the area covered by the official waiting list, then those managing the waiting list should make all reasonable efforts to check with other transplant organisations that the patient is only on one waiting list.

6. Only transplant units recognised by the official waiting list should be able to register patients in their charge on the waiting list and should do so directly with the organisation managing the official waiting list. Patients should be informed that they are on the waiting list and notified if for any reason they are subsequently suspended or removed.

7. There should be a nationally recognised organisation responsible for the management of the waiting list and the allocation of organs. Organs should be allocated on behalf of the transplant units on the basis of objective rules. The allocation rules should be agreed by all the relevant transplant organisations within the geographical area covered by the waiting list.
8. The waiting list should be regularly updated in conjunction with the transplant units. In particular, the situation of suspended patients or those who have been on the list for a long time should be reviewed to make sure they still meet the registration criteria.

9. Allocation rules should ensure that, as far as possible, no group of patients waits longer than another group waiting for the same type of organ. Waiting times should be analysed regularly to ensure that no patient group is disadvantaged. The allocation rules should be changed when necessary to ensure similar waiting times for all groups of similar patients on the waiting list.

10. The organisation responsible for managing the waiting list should provide information, on at least an annual basis, for health professionals and the public. Information should include:
   i. the criteria for registration, the allocation rules and any changes thereto;
   ii. the numbers and flows of patients registered;
   iii. the waiting times on the various transplant lists including:
      a. the actual waiting time for patients who have been transplanted;
      b. the time patients still on the list have waited; and
      c. the average time patients in any group on any organ transplant list can expect to wait.

11. All organisations managing transplant waiting lists should exchange information with comparable organisations to help improve practice. Research should be promoted to analyse and improve the quality of organ transplant waiting lists and waiting time management.

12. Member states should guarantee that a system is put in place for implementing, monitoring and supervising the rules set out in this recommendation.
Explanatory memorandum to Recommendation Rec(2003)10 of the Committee of Ministers to member states on xenotransplantation

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Introduction

The transplantation from humans to humans of organs, tissues and cells has been recognised as a successful therapeutic solution to several previously incurable diseases relating to heart, liver, lung and kidney disorders. Furthermore, this procedure could potentially address other unmet medical needs such as incurable neurological diseases (Parkinson's and Alzheimer's disease), paraplegia due to spinal cord lesions and pancreatic islet or beta cell transplants for treatment of diabetes.

At the moment, most organ transplants are derived from deceased human donors. However, the needs exceed many times the supply and a number of patients continue to die on waiting lists. Because of this acute shortage, some scientists have studied the possibility of transplanting organs originating from animals to human persons, which is referred to as xenotransplantation.

However, because of the particular nature of these animal organs and since there are certain dangers in xenotransplantation which do not exist, or are less clear, in allotransplantation (human to human), additional precautions are necessary for this activity. This is especially the case with respect to immunological difficulties, the potential threat of animal pathogens in humans and intricate issues related to the quality of xenotransplants, animal welfare\(^{(1)}\) and the ethical acceptability of using animals for this purpose. Though some of these difficulties could eventually be overcome, there is still insufficient knowledge concerning the potential risks involved in most of the procedures, such as the transmission of animal pathogens in human beings.
Because of these risks, the *Recommendation on Xenotransplantation* asserts the need for very stringent and demanding conditions whereby no animal to human xenotransplantation should be carried out in a member state that does not provide regulation for such a procedure. This condition is extremely important to protect patients, public health and the animals used. Therefore, if a State does not provide regulation for animal to human xenotransplantation, it should not be allowed to proceed with any clinical intervention be it for research or for any other reason.

During the three years of the Working Party, competing biotechnologies, such as stem cell technology, have been emerging which could potentially address the needs for cell and tissue (but not for complete organ) transplantations. At the moment, it is uncertain whether these new discoveries will have similar or even better prospects than xenotransplantation, particularly with respect to clinical applications.
Drafting of the Recommendation

The Parliamentary Assembly of the Council of Europe, having considered the risks to public health which xenotransplantation could involve asked the Committee of Ministers, on the 29th of January 1999 (Recommendation 1399 (1999) on Xenotransplantation), to initiate a study concerning the different aspects of the relevant issues relating to xenotransplantation taking into account the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (European Treaty Series: ETS No. 164).

The same year, the Committee of Ministers established a Working Party (CDBI/CDSP-XENO) under the joint authority of the Steering Committee on Bioethics (CDBI) and the European Health Committee (CDSP) to evaluate the risks in xenotransplantation and establish appropriate safeguards.

Chaired by Mr. Bart Wijnberg (The Netherlands), the Working Party was composed of Prof. Didier Houssin (Vice-Chair, France), Prof. Annika Tibell (Vice-Chair, Sweden), Prof. Pekka Häyry (Finland), Prof. Karin Ulrichs (Germany), Dr. Marialuisa Lavitrano (Italy), Dr. Dag Sorensen (Norway), Prof. Alexander Tonevitsky (Russian Federation), Dr. Rafael Manez (Spain), Dr. Theodor Weber (Switzerland), Dr. David Cook (United Kingdom), Dr. Maggy Jennings (United Kingdom) and Dr. Line Matthiessen (European Community).

It should be noted that representatives from several non-member states (Prof. Eda Bloom (United States) and Dr. Larry Whitehouse (Canada))
Recommendations of the Committee of Ministers to member states

in addition to several organisations (International Xenotransplantation Association (IXA), OECD, Office International des Epizooties (OIE) and WHO) were active participants, as observers, in the work. Indeed, it was considered that worldwide cooperation between states was necessary in this field and that the participation of representatives of these non-member states and international organisations would enable the drafting of common standards, especially with respect to protecting public health.

The Working Party finalised a draft Recommendation on xenotransplantation in September 2001. In this Recommendation, the Working Party drafted stringent and careful provisions in order to address the concerns expressed by the Parliamentary Assembly. Accordingly, the text states that no animal to human xenotransplantation can be carried out unless sufficient efficacy and safety has been demonstrated. Furthermore, the Recommendation recognises that the xenotransplantation of cells and tissues is already taking place in a number of countries. Therefore, provisions encouraging international co-operation in public health, including with countries where xenotransplantation is prohibited, are incorporated.

The Recommendation is accompanied by this explanatory report drawn up under the responsibility of the Secretary General of the Council of Europe. It takes into account the discussions held in the CDBI and CDSP as well as in the Working Party entrusted with the initial drafting of the Recommendation; it also takes into account the remarks and proposals made by Delegations. The explanatory report is not an authoritative interpretation of the Recommendation. Nevertheless, it covers the main issues of the preparatory work and provides information to clarify the object and purpose of the Recommendation and makes the scope of its provisions more comprehensible.
Protection and guarantees in the field of biology and medicine are provided by the European Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine. In the specific field of transplantation, complementary protection for patients is also given by the Additional Protocol to the aforementioned Convention concerning Transplantation of Organs and Tissues of Human Origin.

Furthermore, the European Convention for the Protection of Vertebrate Animals used for experimental and other Scientific Purposes guarantees protection for animals involved in investigatory procedures including those used in xenotransplantation.

The preamble stresses the importance of the 3rd Conference of European Health Ministers convened in Paris in November 1987 dealing with organ transplantation and also takes due regard to the previous work of the Committee of Ministers and the Parliamentary Assembly of the Council of Europe in the field of transplantation and xenotransplantation.

In addition, the preamble emphasises the importance of considering the work of other national and international organisations relating to xenotransplantation since a communal approach has been recognised as being essential in addressing the relevant issues.
Chapter I

Object, scope and definitions

Article 1 – Object of the Recommendation

1. The aim of the Recommendation is to protect all persons involved in xenotransplantation (patients, close personal contacts and the professional staff involved in xenotransplantation) as well as public health, both in the short term and long term. The provisions also aim to ensure that the welfare of animals used for xenotransplantation is adequately protected. This will include ensuring that source animals are provided with husbandry and care appropriate to their needs and ensuring that the collection of organs, tissues or cells is carried out in a humane manner.

Article 2 – Scope of the Recommendation

2. In the broadest sense, xenotransplantation covers source animals, procurement of organs, tissues and cells, informed consent, surgery and post-operative follow-up and all other activities involving the transplantation of animal parts or human materials which have been in contact with animal parts into human recipients.
Article 3 – Definition

3. Concerning the definition of xenotransplantation:

- The first indent covers the transplantation of parenchymal organs (e.g. kidney, heart, liver, pancreas, lung) and the implantation or infusion of tissues and cells (e.g. skin, bone marrow, blood, pancreatic islets or beta-cells) that have been derived from animals into a human recipient.

- The second indent covers the exposure by a person to human blood or blood constituents that have been in contact with live animal tissues (for example via perfusion), or to human organs, cells or tissues cultured on, or in contact with, live animal cells (regardless of whether they are alive or lethally irradiated but metabolically active), or implanted (stored) in animals.

4. This definition of xenotransplantation includes the transplantation of human stem cell lines and skin cells grown on animal feeder cells but does not include non-living animal products, many of which are regulated as devices (e.g. porcine heart valves), drugs (e.g. porcine insulin) and other biological products (e.g. anti thymocyte globulin, vaccines prepared from animal sources or animal sera used for the culture of human cells).
Chapter II

General provisions

Article 4 – Xenotransplantation – the setting

5. This Article asserts the need for very stringent and demanding conditions whereby no xenotransplantation should be carried out in a member state that does not provide regulation for such a procedure.

6. This regulation should apply the relevant principles of the Convention on Human Rights and Biomedicine\(^{(2)}\), *inter alia* those relating to biomedical research. It should also take into account the specific principles and rules relating to transplantation in particular, which are included in the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin (ETS No. 186) and in The Transplantation Society Recommendation for Legislation in Transplantation\(^{(3)}\). On the other hand, recommendations relating to xenotransplantation can be found in the Transplantation Society’s Recommendation on Xenotransplantation\(^{(4)}\), in the WHO’s recommendation on the Prevention of Infectious Disease in Xenotransplantation\(^{(5)}\), in appropriate US FDA\(^{(6)}\) and PHS\(^{(7)}\) recommendations and other national recommendations when available\(^{(8,9)}\).
7. Because it is extremely important to ensure that patients, their close personal contacts, public health and the animals used are adequately protected, the term “regulation” in this Article includes the requirement for an “authorisation” to be given by a body officially recognised as competent for this purpose before a xenotransplantation takes place.

8. The regulation should cover all aspects of the proposed procedure such as:

   - the collection and maintenance of animal records and the health surveillance plans of the source animals;
   - the genetic manipulation of animals or tissues (where relevant);
   - the procurement of the xenotransplants and the xenotransplantation procedure;
   - the details relating to the qualifications and the necessary scientific and medical expertise of all professional staff involved in xenotransplantation;
   - the management of the recipient and his or her close personal contacts;
   - the criteria for recipient selection and details of the informed consent document;
   - the information programs for the recipient, his or her close personal contacts, the professional staff involved in xenotransplantation and the public;
   - the infection control methodologies;
   - the immunosuppressive regimens;
   - the follow-up time-table and format and the archiving of donor and recipient medical records and specimens.

9. The regulation should also contemplate the possibility of applying constraints such as those mentioned in Article 13.
Article 5 – Xenotransplantation authorisation

Paragraph 1. Clinical xenotransplantation research

10. To maximise the safety of xenotransplantation in clinical research, each procedure should not only fulfil the general conditions applicable to biomedical research and be authorised by a body officially recognised as competent for this purpose but also comply with specific requirements, namely that the intervention is justified having regard to the risks incurred and the potential level of efficacy and safety for the patient and that, in the light of current scientific knowledge it is highly probable that there is no risk, in particular of infection, for public health. In conformity with Article 12, the results from pre-clinical research should also suggest or, where appropriate, the results from prior clinical research indicate that a clear therapeutic benefit for the xenotransplantation recipient exists.

11. As long as xenotransplantation remains experimental, last resort procedures should not be considered as possible exceptions to the requirements applicable to clinical research.

Paragraph 2. Xenotransplantation other than in clinical research

12. When a xenotransplantation activity is no longer considered as medical clinical research, authorisation for this activity should only be given by a body officially recognised as competent for this purpose if there is adequate evidence that no risks, in particular of infection, to the general population exist and it has an established therapeutic utility. One example of xenotransplantation which cannot be considered research, as it has been in clinical use for over 10 years, is the use of human skin cells grown on mouse feeder cells for the treatment of burns patients. Similar techniques may be used to grow limbal cells to repair damaged corneas. Such techniques are of proven clinical effectiveness but do carry a very small risk of transmission of mouse retrovirus and so should be subject to a risk
assessment and proportional patient information and surveillance (see Article 9, paragraph 2).

13. It should be noted that paragraphs 1.a.i and 2.i use two different expressions in relation to the absence of risk for public health. Paragraph 1.a.i uses the expression “highly probable” since indications concerning the absence of such a risk are provided by studies undertaken on animal models; the second paragraph uses the expression “adequate evidence, in accordance with internationally accepted standards” because this evidence is based on research having taken place on human persons. The requirement of a high probability of absence of risks for public health ensures a high level of protection. The wording in paragraph 1.a.i and 2.i is meant to imply that, in accordance to the state of the art, there is no foreseeable risk. In science, however, an absolute certainty cannot be given and there is always the possibility of an unknown risk.

Article 6 – Xenotransplantation teams and centres

14. This Article asserts the need for very stringent and demanding conditions whereby no xenotransplantation should be carried out in a member state unless it is undertaken by an accredited team and in an authorised centre.

Indent a. (xenotransplantation team)

15. The detection, diagnosis and effective treatment of a recipient subject to an infection in addition to the design and implementation of appropriate measures to limit dissemination of a xenosis, if and when it occurs, are only possible in a well co-ordinated xenotransplantation team. Furthermore, in order to address any possible difficulties arising with the animals this xenotransplantation team should liaise efficiently with the source animal production team.

16. In addition to transplant clinicians and associated staff, the xenotransplantation team should include or have access to an infectious diseases physician with expertise in zoonosis,
transplantation and microbiology, a veterinarian with specific expertise in animal husbandry and care issues as well as in infectious diseases of source animals and a hospital epidemiologist/infection control specialist (a team may have more than the indicated number of individuals in order to encompass the necessary expertise). Moreover, the term “appropriately” in indent a) also means that other disciplines such as psychology or counselling can be included. Only once the team is composed of experts having recognised qualifications and the necessary skills and experience in all the required disciplines should the team be officially acknowledged as being competent. Several guidelines, in particular in the United States$^{(10)}$ and Canada$^{(11)}$, describe the necessary composition of the xenotransplantation team. Each member state should specify under which conditions a team may be accredited.

17. The xenotransplantation team should be able to fully explore the proposed project with hospital and university administrations with regards to physical resources, the scale of the initial trials and the ensuing clinical program. Moreover, the legal and financial implications of the activity, including reimbursement methods, storage costs of the samples and overall impact on health care expenditures should be considered.

Indent b. (xenotransplantation centre)

18. Because xenotransplantation should only take place in centres with relevant experience and equipment, in practice it may mean, particularly in the case of solid organs, that only centres already authorised to carry out allotransplantations corresponding to the xenotransplantation procedure to be tested could participate in a xenotransplantation (provided that the additional constraints are satisfied).
Chapter III

Protection of public health

Article 7 – Public Health protection Plan

19. Because there is no room for improvisation in dealing with the risks of xenosis, all provisions and procedures designed to address any events, in particular of infection, possibly related to a xenotransplantation and to react without delay to an event if it occurs, should be thoroughly described in a xenotransplantation plan. These provisions and procedures should include measures to be taken by public authorities to respond to events of transmissible or previously unknown illness possibly related to xenotransplantation. In very exceptional circumstances, such measures might even include the isolation of a patient to prevent any further infections.

20. It should also be noted that, in accordance to Article 32, member states should communicate without delay to national public health authorities of other member states and other concerned states any events, in particular of infection, possibly related to a xenotransplantation, which could compromise public health.

21. Additional information concerning the setting-up of a surveillance framework can be found in the OECD/WHO consultation report on xenotransplantation surveillance\(^{(12)}\) and other WHO reports\(^{(13,14)}\).
22. The surveillance procedures associated with xenotransplantation can only be effective if they are complied with to the letter. The lifelong constraints which may be imposed on some xenotransplantation recipients and their close personal contacts are such that they may conflict with a number of national and international human rights regulations. This is explained in the discussions with the representatives of the European Court of Human Rights (see annex) which states that “[m]any of the rights in the Convention [on Human Rights] were subject to permissible restrictions and involved establishing a proper balance between competing interests.” In particular, the constraints may conflict with the right for one’s medical records to remain confidential, the right to mobility and liberty and the right to refuse the constraints which may arise resulting from the xenotransplantation.

Article 8 – Collection and storage of biological samples and information

Biological samples

23. In order to ensure traceability and long term monitoring, a number of biological samples should be taken from the source animal used in xenotransplantation and the recipients either for immediate testing or for future reference.

a) With respect to the source animal and source herd, guidelines on the breeding conditions of the source animals include a requirement for appropriate regular sampling to monitor the microbiological status of the herd. This is part of the routine procedures to ensure that xenotransplantation material originates from Specified/Designated/Qualified Pathogen-Free animals.

b) Appropriate blood/tissue samples of the source animal should also be kept indefinitely for future reference. The United States PHS Guideline on Infectious Disease Issues in Xenotransplantation describes in a specific paragraph “Archives or Source Animal
Medical Records and Specimens” the desirable samples and conditions for storage.

c) Provisions should be made for the monitoring of the personnel caring for the animal, the patient, his or her close personal contacts, and the medical and non-medical staff in charge of the patient’s care. In relation to the specific xenotransplantation procedure to be tested, the details concerning who is eligible for monitoring, the frequency of such monitoring and the tests to be performed should be determined in advance.

d) In addition, a number of samples should be collected and archived for potential future reference. A proposed patient sampling schedule is given in the United States guideline. According to this document, specimens appropriate to the specific xenotransplant situation, and including systematically blood, plasma and peripheral mononuclear cells, should be collected:

a. every month (or as much apart as possible) before the xenotransplantation,
b. immediately after the xenotransplantation period,
c. approximately 1 month and 6 months post xenotransplantation, then
d. annually for the first 2 years and, finally,
e. every 5 years for the rest of the recipient’s life.

24. Specimens of any xenotransplant that is removed (e.g. post-rejection) should be banked. Additionally, it is recommended that specimens of the xenotransplant, serum, blood, white blood cells, and samples of the patient should be stored after his or her death. These specimens should undergo appropriate histological, microbiological and viral assays. Snap-frozen tissue samples, paraffin embedded tissue and tissue suitable for electron microscopy from the xenotransplant and all major organs should be stored.
Recommendations of the Committee of Ministers to member states

Health care records

25. The following records should be established and archived:
   – an institutional xenotransplantation record;
   – a record of hospital acquired infections which may have occurred because of the xenotransplantation;
   – individual xenotransplant recipient medical records.

National Registry

26. All countries where xenotransplantation is performed should establish a national registry. Archiving of samples of sera, plasma, leukocytes and tissue of the source animal and recipient should be included in all national guidelines for xenotransplantation.

Article 9 – Follow-up

Paragraph 1. Clinical xenotransplantation research

27. A plan ensuring the traceability and monitoring of recipients, close personal contacts and professional staff involved in xenotransplantation should be set up. This plan should include the collection and storage of information and biological samples from recipients in accordance with Article 8. The existence of this plan is important in order to detect and deal with any infections possibly related to xenotransplantation and any other complications of relevance to public health. Because of the potentially serious implications of contagion in particular, the plan should also ensure that public authorities are alerted without delay of any events, in particular of infection, possibly related to xenotransplantation.

28. The Article does not define the term “adverse event” as such but this term is meant to imply any adverse incident or occurrence, relevant that is possibly related to the xenotransplantation. An adverse event does not only relate to infections but might also cover incidents such as the appearance of a prion disease. The
requirement to communicate information on all such events to the national public health authorities ensures that those authorities will be able to make a judgment on the possible relevance of the event to public health, rather than such a judgment being made by the research team.

Paragraph 2. Xenotransplantation other than in clinical research

29. Because some xenotransplantation procedures, such as the use of human skin cells grown on animal feeder cells in the treatment of burns victims, have already been used for many years without any evidence of infectious events, the constraints associated with these procedures would only be required insofar as they are necessary and in accordance with the principle of proportionality. It has been recognised that these cells do not pose the same potential risks as some other xenotransplantation interventions and therefore need not be subject to all of the precautions of other xenotransplantation procedures, but that some of them are still appropriate (e.g. recipient notification of the use of mouse cells, initial archiving of recipient samples and passive monitoring, archiving of samples, databasing of recipients, etc.). However, because it is impossible to foresee all possible consequences of an intervention, a plan should also be set up for xenotransplantation other than in clinical research to ensure that public authorities are alerted without delay of any events, in particular of infection, possibly related to such a procedure which could be of relevance to public health.

Article 10 – Precautions relating to the transmission of disease

General considerations

30. It is recognised that one of the key safety issues in xenotransplantation is the risk of xenosis for the recipient with the theoretical possibility of a new, contagious, disease emerging in the human species. Such a scenario is only possible if:
Recommendations of the Committee of Ministers to member states

- a potentially pathogen micro-organism is transmitted to the recipient;
- this micro-organism is adapted or adapts to its new environment (the recipient);
- the micro-organism multiplies in the recipient;
- the micro-organism causes a disease;
- inter-human transmission of the micro-organism occurs;
- the (possibly new) micro-organism is also infectious and pathogenic to a section of the population which is large enough to allow its dissemination.

31. Possible actions to minimise such a risk are:

- selection of the source animal species to minimise the risk of xenosis;
- control of the microbiological quality of the xenotransplant;
- prevention of infection in the xenotransplant recipient;
- detection, diagnosis and effective treatment of a possible infection in the recipient;
- limitation of the infection by education and surveillance of the recipient, his or her close personal contacts and any potentially infected person;
- warning without delay in the event that a significant public health hazard is identified, so that appropriate measures can be taken worldwide.

32. Many known micro-organisms which might cause xenosis can be eliminated from the xenotransplant material by the use of appropriate source animal breeding and husbandry conditions, microbiological screening, and organ, cell or tissue procurement procedures. For these reasons, prior to any xenotransplantation authorisation, the breeding and husbandry conditions and procedures, the source animal screening procedures and the xenotransplant procurement and preparation procedures should be thoroughly documented and checked for compliance with
appropriate microbiological quality requirements (e.g. qualified pathogen-free). Additionally, a microbiological monitoring and surveillance system encompassing all the stages from the production of the source animals to the final collection of the xenotransplants, should be constantly maintained.

Quality Assurance

A Quality Assurance system should be set up encompassing:

1. All the stages of production of the source animals

33. Breeding source animals devoid of a number of pre-defined microorganisms (so-called Specified/Designated/Qualified Pathogen-Free animals), and minimising the risk of external contamination of the source animals or xenotransplants are important. Complex technical recommendations have been or are being elaborated, e.g. in Canada (proposed Canadian Standard for Xenotransplantation), in the United States (PHS Guideline on Infectious Diseases Issues in Xenotransplantation) and in the UK.

34. Xenotransplantation source animals should be from lines maintained in biosecure facilities over several generations. The health (specified/designated/QPF) status should be maintained during movement and transport.

35. Pre-clinical screening of source animals should include the most advanced methods for detection of potential infectious agents (bacteria, viruses, prions, parasites and fungi). Microbiological screening should be species-specific and characterise the potential infectious agents for humans. Testing for endogenous retroviruses, persistent viral infections and prions should be considered based on the available technology for such studies.

36. Source animals should come from closed herds or colonies maintained in biosecure facilities under experienced veterinary supervision practising the highest quality of veterinary care. The animals should be screened and qualified as pathogen-free for specific agents as appropriate for the clinical application and
be maintained in an environment that minimises exposure to infectious agents and their vectors whilst taking account of their husbandry and care needs as set out in Article 23.

2. The final collection of the xenotransplants

37. Xenotransplanted cells, tissues or organs should be procured with a documented aseptic methodology in facilities meeting the highest surgical standards. Where possible, xenotransplants should be tested repeatedly both before and at the time of xenotransplantation for contamination by infective agents with standard and co-cultivation assays, the latter including appropriate indicator cells and cell lines derived from human peripheral blood mononuclear cells and cells from the xenotransplantation site (e.g. Central Nervous System, bone marrow, etc.).

Hospital infection control

38. Standard biohazard precautions should be maintained. When the source of a significant illness in a recipient remains unidentified despite standard diagnostic procedures, comprehensive testing of body fluid and tissue samples using validated culture systems, genomic detection methodologies and other advanced techniques should be undertaken. Archiving of acute and convalescent sera and blood cells is also important. An occupational health services program for professional staff involved in xenotransplantation should include an education program together with worker surveillance protocols. Protocols should be established for post-exposure (e.g. needle-stick, splash, mucous membrane exposure) evaluation and management.

39. Should a potential xenogeneic infection related to a clinical episode occur, an epidemiological investigation to assess the potential public health significance of the infection should be initiated without delay in co-ordination with the appropriate public health authorities.
Article 11 – Prohibition relating to the use of non-human primates

Paragraph 1

40. It is presently acknowledged, worldwide, that non-human primates (macaques, baboons, etc.) should not be used as source animals for human xenotransplantation until more information is obtained, allowing a better assessment of the infectious risks. This position is developed in a specific US Food and Drug Administration Guidance Document entitled *Public Health issues posed by the use of non-human primate xenografts in humans*\(^{(21)}\). Further reasons to prohibit the use of non-human primates as a source species are the serious welfare implications of maintaining these primates in biosecure conditions together with the wider ethical implications of their use.

In Sweden, for example, because of concerns relating to the involvement of non-human primates in xenotransplantation, the Swedish Committee on Xenotransplantation, in their 1999 report, has explicitly banned their use as a source species\(^{(22)}\). Similarly, the proposed Canadian Standard for Xenotransplantation states that despite the greater immunological proximity to humans of primates (absence of preformed antibodies, and therefore, of xenotransplant hyperacute rejection), their use as source animals is not feasible. This is because the phylogenetic proximity of humans to other primates is suspected to increase the probability of xenosis.

Paragraph 2

41. Though non-human primates should not be used as source animals, it should be noted that the literature\(^{(23,24)}\), shows that Vero cells (long ago obtained from African Green Monkey kidney cells) have already been used in Switzerland as a vehicle to transfer a gene (interleukin-2) to cancer patients. In addition, there is an *in vitro* fertilization technique used in France in which a Vero
cell feeder layer is used\textsuperscript{(15,16,17)}. In this technique, co-cultures of human embryos, particularly with Vero cells, are used mainly in cases of successive failures of implantation. Thus, the use for xenotransplantation of cell lines obtained from non-human primates may be permissible if substantial evidence addressing the infectious disease risks, ethical issues and animal welfare concerns is supplied to the appropriate body (see Article 5), and the said body determines that the evidence is sufficient. However for some types of non-human primates, such as the Great Apes, it is envisaged that no permission for their use as source animals should be given because of serious ethical and animal welfare concerns.
Chapter IV

Protection of patients and close personal contacts

Article 12 – Conditions for patient participation

42. This Article builds on the previous very stringent and demanding conditions whereby no xenotransplantation should be carried out in a member state unless regulation for xenotransplantation activities exists and sufficient efficacy and safety is demonstrated through pre-clinical research.

43. The need for the pre-clinical demonstration of efficacy and safety of the planned therapeutic procedure is not specific to xenotransplantation. These requirements are generally applicable to any new therapeutic procedure being submitted to a clinical evaluation which should establish that the expected benefits outweigh the risks of the procedure.

44. This principle is stated in the European Convention on Human Rights and Biomedicine of the Council of Europe (ETS No. 164) which states in Chapter V (Scientific research), Article 16, indents i and ii, that: “Research on a person may only be undertaken if (i) there is no alternative of comparable effectiveness to research on
humans and (ii) the risks which may be incurred by that person are not disproportionate to the potential benefits of the research”.

45. The objective of pre-clinical research is to quantify, as far as possible, the expected benefits as well as the potential risks to the subject in such a way that the physicians in charge of the patients, the ethics committees and the patients themselves are in a position to make a decision which is as rational as possible. The expected benefits should be carefully weighed against the potential risks, whether quantifiable or not (i.e. a given risk can be foreseeable though not quantifiable), because the nature and level of acceptable risks will depend on the nature and magnitude of the expected benefits.

**Specific aspects relating to xenotransplantation**

46. In the above key statement of the European Convention on Human Rights and Biomedicine, it is generally considered that the potential benefits of the clinical research may assist either the research participant or other persons (e.g. future patients), or both, but that any risks may only concern the research participant.

47. However, in the field of xenotransplantation, another dimension has to be considered in the decision making process, namely the potential risks to persons other than the patient being treated. These potential risks are mainly of an infectious nature and are, at present, not adequately quantified. They concern (a) the close personal contacts of the xenotransplant recipient and (b) the population at large, with the theoretical possibility of a new disease emerging as a consequence of xenotransplantation. Such a scenario may only occur if a transmitted micro-organism becomes capable of causing a human disease (although there could be a long latency between infection and disease symptoms). Therefore, no xenotransplantation activity should be carried out unless there is adequate evidence, in accordance with internationally accepted scientific standards, that no risks, in particular of infection, to the general population exist.
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*Therapeutic results expectations*

48. The pre-clinical evaluation of efficacy and safety of the proposed xenotransplantation should be addressed separately. However, it is emphasised that any decision to proceed or not with a given xenotransplantation should be based on the evaluation not only of efficacy and safety, but also on a thorough evaluation of the acceptability of a certain level of potential risks, both to the patients and to others, given the level of expected benefits to the patients of the planned study.

Indent i. Absence of appropriate alternatives

49. Xenotransplantation should not take place if other therapeutic procedures of comparable effectiveness are available for the patient. Indeed, in view of the risk involved in any xenotransplantation, there is no justification for using this procedure if there is another appropriate way of bringing the same benefit to the recipient, such as “conventional” treatment, or tissues of human origin, cultured tissues or tissues transplanted from the recipient. When an appropriate organ or tissue of human origin (allotransplantation) becomes essential to a patient, the shortage of such elements could justify having recourse to xenotransplantation if all other conditions are fulfilled.

50. For patients with acute organ failure, it is often difficult to obtain a suitable allotransplant. Xenotransplantation may in this case provide the best available therapy. The xenotransplant could then either be a permanent solution or be performed as a bridging procedure until a human transplant becomes available.

51. In case of non life-saving procedures, such as renal transplantation, xenotransplants might increase the number of organs available for transplantation and may possibly also increase the transplantation possibilities of patients that are highly sensitised against human tissue and have developed antibodies to the majority of human HLA-antigens.
52. Some diseases causing organ failure are likely to re-occur in the transplanted human organ. The use of a xenotransplant may in some cases reduce this risk since so-called species-specific disease resistance may exist.

53. Xenotransplantation has also been suggested for diseases that are only rarely treated by allotransplantation. Attempts to treat these diseases may use, for example, neuronal cells from fetal tissue which must be procured from the fetus during a very specific developmental stage. In some countries, the use of human fetal material has been explored while in others this is not considered to be acceptable. Besides the ethical problems, the aborted tissue is often of suboptimal quality.

54. The use of xenogeneic material, on the other hand, may provide a possibility to optimise the procurement technique which may improve the quality of the cells. It might also serve to improve the ability of medical staff to prepare and plan xenotransplantation procedures while at the same time providing a larger accessibility to xenotransplant material. Furthermore, xenotransplantation avoids some of the ethical problems connected with the use of tissue from human aborted fetuses.

55. As in any other clinical procedure, patients should be selected amongst those for whom the likely benefits outweigh the potential risks. Considering the lifelong surveillance and lifestyle restrictions that may be necessary in xenotransplantation it is reasonable to reserve xenotransplantation for serious or life threatening disorders. Another prerequisite should be that safe and effective alternative treatments have not been developed or are not available to all the patients in need. The International Society for Heart and Lung Transplantation, at their April 2000 meeting in Osaka, Japan, made public a set of recommendations on patient selection criteria and experimental prerequisites to heart xenotransplantation. These can also serve as a basis for setting up requirements.

56. It should be noted that the consideration of a xenotransplantation procedure may evolve with time and that this should be taken into
account in indent i. Indeed, some procedures may eventually be considered as safe, while others are set aside, with the accumulation of experience.

Indent ii. Data suggesting suitable efficacy

57. The expression “clear therapeutic benefit” should be defined for the individual xenotransplantation proposed and the term should be interpreted to cover a number of benefits in different fields. However, the importance of these benefits should always be weighed against the risks for patients and for society.

First indent

58. The precise technical requirements to demonstrate sufficient efficacy of the proposed xenotransplantation can only be addressed on a case by case basis. Precise requirements have not been laid down in individual countries. However, the Xenotransplantation Commission of the Spanish Committee of Transplants, in their 1998 recommendation(29), has proposed the following “indispensable requirement” in terms of pre-clinical efficacy: “Survival and adequate function of the cells, tissues or organs grafted during a period of at least 6 months.” This statement can serve as a broad basis for further elaboration because it indicates that a sufficient pre-clinical period for demonstrating efficacy should be required. However, the following should also be taken into account:

- the nature of the xenotransplant (e.g. whole organ such as heart, isolated cells such as dopaminergic neurons, tissues such as pancreatic islets, etc.);
- the performance level of the xenotransplant required to reach the expected benefit (stage of differentiation or growth, metabolic functions, secretions, ability to proliferate, physiological regulations, etc.);
- the medical condition of the potential human recipients;
- the prognosis of the condition to be treated in the absence of a xenotransplantation (i.e. with conventional treatments);
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- the source animal species;
- the recipient animal species and its relevance to the prospective xenotransplantation;
- the data pertaining to the quality of life of the recipient animals and their relevance to the xenotransplantation (e.g. level of immune suppression, side effects of the concomitant treatments, global physiology of the recipient, etc.)

59. The use of animal models is important in demonstrating adequate function of a xenotransplant, and it is recognised that the use of non-human primates is likely to be necessary at some stage in the development programme before the procedures are approved for use in humans. However it is expected, in accordance with the provisions of Convention ETS No. 123 of the Council of Europe and Directive 86/609/EEC of the European Union that animals will only be used where there is no alternative, and that non-human primates in particular will only be used where no other suitable species is appropriate. In general, progression to non-human primate studies should only follow a thorough and critical assessment of the need to use these species, including a detailed evaluation of in-vitro development work and, where appropriate, development work in other animal models. Every effort should be made to limit the duplication of research on any species, and to refine the use of animals, for example by improved husbandry and care practices. The programme should be subject to continuous review to ensure that animal use and suffering is minimised. In this context, it is generally accepted that non-human primates should not be used as source animals, both because of cross-species infection risks and because of the serious welfare implications of keeping these animals in biosecure facilities (see Article 11). However, it is recognised that the use of non-human primates as models is necessary to the pre-clinical evaluation of the efficacy of xenotransplantation, especially in terms of whole organ transplantation. The pre-clinical use of animals as recipients, and particularly non-human primates, is another factor to take into consideration when defining the period of time required for demonstrating safety and efficacy. This period
should be sufficient to allow both demonstrative and convincing assessment but also calculated to minimise, as far as possible, the suffering caused to the animals.

60. The American Society for Testing and Materials issued draft guidelines for discussion in which the pre-clinical requirements for tissue and cell products, whether allogeneic or xenogeneic, are outlined. The three classical aspects of therapeutic products, i.e. quality, safety and efficacy, are considered. These can also serve as a basis for further elaboration.

Second indent

61. A transplant from a distant species, such as a pig, to a human person elicits a very strong response, termed hyper-acute rejection whereby the organ turns into a black, swollen, useless mass, within several minutes or hours. Moreover other rejections exist such as acute vascular and cellular rejections which may occur within days of transplantation and chronic rejection which may suddenly appear months or even years after the operation. This provision states, therefore, that pre-clinical studies should provide sufficient reasons to believe that the problems related to rejection can be overcome.

Indent iii. Risks related to xenotransplantation

62. In any medical procedure such as xenotransplantation, the risks to the patient should be properly evaluated and should be balanced against the potential therapeutic benefits which may result (principle of proportionality).

63. Moreover, xenotransplantation should only take place if it is expected to provide better results than other therapies available to the patient. In this context, better results should be interpreted to cover several possibilities, for example, xenotransplants cannot be expected to provide better results than the survival rates currently obtained with human allotransplants.
Infectious risks of xenotransplantation

64. Xenotransplantation creates particular conditions where transmission of known or unknown pathogens from source animal to human recipient becomes a possibility and might ultimately become a public health risk. A number of factors contribute to this situation since:

– the transplantation bypasses the recipient’s normal physical protective barriers;
– the recipient, in many cases, will be in an immuno-compromised state in order to promote xenotransplant acceptance;
– the recipient will be continuously exposed to a xenotransplant in which pathogens may be present, thereby increasing the risks of the micro-organisms adapting to the human species;
– clinical recognition of a previously unknown, possibly slow-developing, disease may be difficult;
– laboratory tests may be inadequate or lacking altogether.

Need for experimental data to evaluate the risk of xenosis

65. Even under the most stringent conditions, a number of potential pathogens, in particular certain viruses, cannot be eliminated. Of particular concern are (a) retroviruses, especially endogenous retroviruses, which constitute part of the genome of the source animals, and (b) prion diseases. Therefore, because infectious risks cannot, at present, be completely eliminated through animal breeding techniques, the screening of source animals and the xenotransplant procurement procedures, it is necessary that the planned xenotransplantation should have been thoroughly tested experimentally. Thus, tests studying the potential for xenotransplantation to cause infectious diseases in the recipients should be performed during a sufficiently long period of time without any evidence of an increased risk being observed. In this respect, any research involving animals should fully address the
relevant ethical and animal welfare concerns and comply with relevant regulations (such as Convention ETS No. 123). These issues are further addressed in Chapter V of the Recommendation relating to the protection of animals.

66. In the event of any transmissions of an infectious agent arising, an appropriate monitoring period should be required to evaluate the consequences. As an example, the Spanish Xenotransplantation Commission, in their 1998 Recommendation\textsuperscript{(31)}, have proposed the following three “indispensable requirements” to demonstrate pre-clinical safety:

- Demonstrated an absence of transmission of infectious agents in the recipient animal during a period of at least 6 months.
- Demonstrated an absence of any non-accidental transmission of infectious agents to the caretakers and other personnel involved in the research programme.
- Demonstrated, in the case of transmission of any infectious agents, that a minimum follow-up of one year has been carried out to evaluate the consequences both to the recipient and to the other animals in contact with the source animal.

However, the limited number of pre-clinical testing studies that good research practice recommends when using animals, and particularly non-human primates, entails that the lack of transmission of infectious diseases from the source animal to the recipient will not rule out completely a risk of xenosis. Thus, the consequences for the recipient of known infectious agents present in the source animal which cannot be excluded by the pathogen-free qualification should be explicitly investigated.

Non-infectious risks

67. Non-infectious risks should be explored in the pre-clinical xenotransplantation investigations. The details should be addressed on a case by case basis. Appropriate data should be provided to assess in particular:

- the risks linked to the immunological manipulation of the recipient and/or of the xenotransplant;
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- the risks linked to the physiological adaptation of the xenotransplant to its new environment;
- the potential psychological or sociological risks to the recipient and/or his or her close personal contacts.

**Article 13 – Information to be given to patients**

68. Information given to the patient is an essential element for the validity of his or her consent. Paragraph 1 of this Article enunciates the general content of the information to be provided. Paragraph 2 addresses issues specific to information on xenotransplantation procedures.

**Paragraph 1**

69. Patients participating in a xenotransplantation should be adequately informed in a comprehensible manner of the nature, objectives, possible benefits, potential risks and consequences of the procedure, as well as of any constraints that may be linked to it.

70. It is important to ensure that patients are given all the appropriate information which should be presented in an unbiased manner and in a way that should easily be understood by lay people. During the decision making process, the patient should have access to discussions both with independent experts not involved in the proposed xenotransplantation and members of the team.

**Paragraph 2**

71. The patient should be informed of the constraints associated with the specific xenotransplantation procedure that he or she is planning to undergo.

72. This paragraph lists the most relevant personal constraints, which may directly affect the patient. The constraints will vary, in conformity with the principles of necessity and proportionality, depending on the nature and the circumstances of the procedure.
If a specific xenotransplantation procedure has already been used as a clinical treatment for a sufficiently long period of time and if there is sufficient evidence to show that this procedure is safe, the constraints would be proportional to the risks perceived. This would happen, for example, for burns patients using human skin cells grown on animal feeder cells. If, on the other hand, a specific xenotransplantation procedure remains an experimental activity or is in clinical practice but continues to be perceived as being associated with high risks, then the patient should be informed of the more stringent constraints associated with the procedure.

73. Paragraph 2b) addresses the requirement for the patient to provide information to the medical team concerning his or her current close personal contacts so that, where there is a need to do so, they may also be made aware of the risks of infection and the constraints associated to xenotransplantation.

If the patient does not agree to his or her close personal contacts being informed when it is considered there is a need to do so then the xenotransplantation should not take place.

74. Because of the potential risks of infection and the possible constraints resulting from these risks, paragraph 2g) specifies that the patient should, where necessary, also be notified, and agree that, a medical team should provide future close personal contacts with information which may help them respond to xenotransplantation concerns. Thus, it would be the recipient’s responsibility to put future close personal contacts in relationship with an appropriate medical team having experience in xenotransplantation so that they may be given this information. The requirement for patients to agree that appropriate information is provided to future close personal contacts is important since the xenotransplantation team may not be aware of the existence of these contacts (see Article 14).

75. Documented informed consent and recipient education should include, in addition to the constraints presented in Article 3, paragraph 2, information on the following:
the known and unknown potential for infection by zoonotic agents and the unknown risk of transmission of xenogeneic infectious agents to the recipient’s close personal contacts;

- the need for isolation procedures during hospitalisation and their nature;

- the possibility of future isolation which may become necessary in the event of a contagious or previously unknown illness occurring;

- the fact that immunosuppressed persons may be at an increased risk of xenogeneic infection and that specialised precautions (e.g. dietary, personal, travel) may be required following hospital discharge;

- the need for the patient to comply with long-term (potentially lifelong) surveillance necessitating routine physical evaluations with archiving of tissue and/or serum specimens including the schedule for clinical and laboratory monitoring;

- the need for any serious or unexplained illness arising in the recipient or his or her close personal contacts to be reported to a physician without delay;

- the unknown impact of possible psychological or social problems for xenotransplant recipients, their close personal contacts or other individuals in society;

- the possibility that in the event of death, the need for a complete autopsy may exist;

- the requirement that recipients should never donate blood, or any blood constituent or any other body fluid, tissue or part for use in humans.

Paragraph 3

76. The special constraints which may be connected with xenotransplantation should be explained repeatedly and in detail since they may conflict with a number of national and international human rights regulations. This is explained in the discussions with the representatives of the European Court of Human Rights (see
Recommendations of the Committee of Ministers to member states

annex) which states that “[m]any of the rights in the Convention [on Human Rights] were subject to permissible restrictions and involved establishing a proper balance between competing interests.” It should also be noted that restrictive measures such as quarantine procedures are not specific to xenotransplantation but are also applied for other contagious illnesses when they occur. The possibility for the state to intervene and take coercive measures should be discussed and assessed with respect to the national legal situation.

Article 14 – Information to be given to close personal contacts of the patient

77. In contrast to most other therapeutic procedures, xenotransplantation has direct consequences on the lifestyle of the patient's close personal contacts. Thus, in accordance with Article 16, paragraph 1, indent ii, the patient should be aware that he or she should, where required, provide to the medical team the necessary information concerning his or her current close contacts. Furthermore the patient should accept that his or her current and future close personal contacts may need to be informed of the envisaged xenotransplantation and of the risks and constraints possibly associated with such a procedure. This is especially important with respect to the measures to be taken to minimise potential infections (Spain(32), Canada(33), United Kingdom(34), United States(35)).

However, this information should only be provided by the medical team to the close personal contacts if the patient has given his or her informed consent to such a course of action; if the patient refuses to authorise the provision of such information, the xenotransplantation should not be carried out (see comments on Article 16, paragraph 1, indent ii).

78. In this Article close personal contacts can be described as persons who have “engaged in activities that could result in intimate
exchange of body fluids”\((36)\). For example, close personal contacts could include:

- persons with whom the recipient is having sexual contact without protection,
- persons with whom the recipient is exchanging blood or saliva,
- children which are breast-feeding from a xenotransplant recipient,
- “household members who share razors or toothbrushes”\((36)\), and
- “health care workers or laboratory personnel with repeated percutaneous, mucosal or other direct exposures.”\((36)\)

At the same time, the FDA draft guidance document entitled “Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Intimate Contacts”\((36)\) indicates that the “[s]haring of housing or casual contact, such as hugging or kissing without the exchange of saliva, would not be interpreted as intimate contact.”

79. It is also desirable that the recipient and close personal contacts should never donate body fluids or body parts for use in humans following a xenotransplantation. Such a requirement is explicit in the United States and Canadian documents\((37,38)\).

80. If a close personal contact refuses to listen or abide to the information given by the medical team, then the medical team should consider whether the xenotransplantation should take place on a case by case basis. It should be noted, however, that with respect to xenotransplantation research, a specific right to participate in such a procedure does not exist.

81. If the close personal contact and the patient begin a relationship after the xenotransplantation, it is the patient’s responsibility to provide information to be given to the close personal contact or to ensure that this information is otherwise provided. For example, the patient should inform any future close personal contacts of the possibility of obtaining additional information from a medical team.
Article 15 – Information to be given to the professional staff involved in xenotransplantation

82. Because professional staff involved in xenotransplantation may also be exposed to infectious agents, it should be ensured that these professionals are fully aware of the potential risks and consequences related to such a procedure including possible constraints associated with their involvement in the procedure.

Article 16 – Consent to xenotransplantation

Paragraph 1

Indent i

83. No person should undergo xenotransplantation without his or her free and informed consent. A patient's consent is considered to be free and informed if it is given on the basis of objective information as to the nature and the potential consequences (including any necessary specific constraints) of the xenotransplantation and its alternatives, in the absence of any pressure from anyone. Information on the risks involved in the xenotransplantation and in alternative courses of action should cover not only the risks inherent in xenotransplantation but also any risks related to the individual characteristics of each patient, such as age or the existence of other pathologies.

84. Often, the decision to consent to a procedure will influence the lifestyle of the patient and his or her close personal contacts including the requirement for lifelong surveillance and the possibility of extensive coercive measures. The legal basis for the performance of lifelong surveillance of patients will probably differ between countries but, in most cases, a strong suspicion or a definite demonstration of a potential risk is likely to be necessary.

85. Information relevant to consent should be presented and explained to the patient or, if the patient does not have the
capacity to consent, the next-of-kin (or person(s) responsible) by an independent person, such as a patient advocate (helped, if necessary, by an interpreter) who is not a member of the xenotransplantation team. The patient or the next-of-kin (or person(s) responsible) should have enough time to consider the information and always more than 24 hours before the proposed xenotransplantation.

Indent ii

86. Xenotransplantation should not be carried out without the provision by the patient to the medical team of the necessary information concerning his or her current close personal contacts. The patient should also accept that his or her current and future close personal contacts may need to be given the information mentioned in Article 14 by the relevant medical team so that they may also become aware of the risks of infection and the constraints associated to xenotransplantation.

Paragraph 2

87. Freedom of consent implies that consent may be withdrawn at any time prior to a xenotransplantation and that the decision of the person shall be respected once he or she has been fully informed of the consequences. However, this principle does not mean, for example, that the withdrawal of a patient's consent once he or she has been exposed to the animal material should always represent an end to the possible constraints mentioned in Article 13. Because of the risks of infection, a state may indeed impose constraints to protect public health.

Article 17 – Counselling and support

88. Xenotransplantation is a very complex process involving not only medical but also ethical, psychological and social aspects. Because of this, the patients and their close personal contacts should be
given proper information and have access to counselling and support that is individually adapted to the patients' and their close personal contacts' backgrounds and previous experiences. It is also important that patients and their close personal contacts be given appropriate updates on developments in xenotransplantation and have long-term access to counselling in addition to education about xenotransplantation and its consequences.

**Article 18 – Right to medical care**

89. The decision whether or not to participate in a xenotransplantation should be taken without any fear that a refusal to participate in the procedure would jeopardise the possibility of obtaining good medical care or lead to impaired relations with the medical team in the future. This is a prerequisite when approaching patients for participation in any clinical procedure including xenotransplantation. Even if it may seem obvious to the clinician or investigator, it is important that this is made clear to the patients and their close personal contacts so that inappropriate pressure during the decision making process is avoided.

90. Though xenotransplantation can be used for some patients instead of allotransplantation, a refusal to participate or a withdrawal from a xenotransplantation should not prejudice a patient's right to benefit from an allotransplant if medically indicated. Similarly, if a suitable human transplant becomes available after a patient has consented to participate in a xenotransplantation, the patient should still be considered for an allotransplantation. If a patient has been removed from the allotransplant waiting list because of a xenotransplantation which eventually proves unsuccessful, the patient should be put back on the waiting list without the xenotransplantation having influenced the patient's position on the list. A patient could of course still be given priority, with respect to an allotransplant, for medical reasons.
Recommendations of the Committee of Ministers to member states

Article 19 – Patients not able to consent

Paragraph 1. Xenotransplantation other than in clinical research

91. Xenotransplantation other than in clinical research for patients not able to consent should only be allowed if there is no therapeutic alternative of comparable effectiveness available to the patient. Moreover, for patients unable to consent, xenotransplantation should only be authorised if there is adequate evidence, in accordance with internationally accepted scientific standards, that no risks, in particular of infection to the general population, exist and the therapeutic benefit of the xenotransplantation has been established as indicated in Article 5, paragraph 2.

92. Because of the specific vulnerability of patients unable to consent this Article also specifies that they may only be included in a xenotransplantation other than in clinical research if the intervention is expected to result in a direct and important benefit for the patient which would offset the constraints and conditions to which the person will or may be subjected according to Articles 13 and 14. Furthermore, the representative or an authority or a person or body provided for by law, after receiving the information referred to in Article 13, should have authorised both the intervention and the provision of the necessary information to the present and future close personal contacts of the patient.

Paragraph 2. Clinical xenotransplantation research

93. As a principle, a patient incapable of giving informed consent should not undergo clinical xenotransplantation research. Only under exceptional circumstances, and when there is adequate indication, on the basis of prior clinical research, that the clinical xenotransplantation research procedure might be lifesaving and there is no alternative means of saving the life of the particular patient unable to consent, should it be considered. Under all circumstances, the intention to include patients incapable of giving
informed consent should be clearly stated in the application to the xenotransplantation body defined in Article 5 and should be specifically considered during the authorisation procedure.

94. Because of the specific vulnerability of patients unable to consent this Article also specifies that they may only be included in clinical xenotransplantation research if the intervention is expected to result in a direct and important benefit for the patient which would offset the constraints and conditions to which the person will or may be subjected according to Articles 13 and 14. Furthermore, the representative or an authority or a person or body provided for by law, after receiving the information to be given to the patient referred to in Article 13, should have authorised both the patient’s participation in the clinical xenotransplantation research and the provision of the necessary information to the present and future close personal contacts of the patient.

95. Though it is important that patients unable to consent should be protected against undue experimentation, it has also been pointed out that such patients should have a right to be involved in research related to problems that cannot be studied in other groups. These patients would, otherwise, be excluded from the development of new treatment strategies.

**Article 20 – Confidentiality**

96. Personal data concerning the recipients and their close personal contacts should be treated as confidential and handled in accordance with the rules on personal data protection. Here, the principles laid down in the *Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data* of 28 January 1981 (ETS No. 108) should be observed. In particular, Article 5.b of this Convention provides that personal data are “stored for specified and legitimate purposes and not used in a way incompatible with those purposes”. Parties should take account of other national or international instruments, such as Recommendation (97) 5 of the Committee of Ministers to the member states on the protection
of medical data and, where applicable, Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on free movement of such data.

97. In xenotransplantation, it is nevertheless essential that the principle of confidentiality should not prevent the medical team involved in any procedure from obtaining the necessary information on the recipient and their close personal contacts, subject to appropriate safeguards to ensure adequate data protection.

**Article 21 – Compulsory constraints**

98. An infectious event related to a xenotransplantation is a complication that not only affects the patient but may also pose a risk to close personal contacts, professional staff involved in xenotransplantation and even to the general public. Because of this, and when a xenotransplantation has already been carried out, a state may intervene, in accordance with national law and the principles of necessity and proportionality, if the patients or their close personal contacts refuse to comply with the agreed surveillance, lifestyle restrictions or treatment schedules. It is important that patients and their close personal contacts are fully informed of the nature of such an intervention. States should also have regulations in place relating to xenotransplantation which take into account the risks of infectious disease as stated in the provisions relating to Article 4 of the Explanatory Report.

99. Patient compliance with surveillance and lifestyle restrictions will greatly influence the risk for the public if a transmission of a microbiological agent occurred. It is thus very important that patients involved in xenotransplantation are likely to be compliant with the xenotransplantation regulations. Non-compliance with immunosuppressive medication and the postoperative follow-up is today one of the most common causes for renal graft loss in many countries. Special care should be taken in this respect and psychological evaluations should be included in the selection process.
Chapter V

Protection of animals

Article 22 – Compliance to animal protection regulations

100. A source animal is an animal that will provide cells, tissues or organs for use in xenotransplantation. The animals used to provide eggs or sperm in the breeding programme to produce source animals are generally referred to as dams or sires respectively.

101. Source animals for xenotransplantation will be reared under highly specialised conditions comparable to those for laboratory animals. They are likely to be derived using techniques designed to improve and maintain their microbiological status which give rise to associated welfare concerns. Source animals should also have to undergo scientific procedures (e.g. blood and tissue typing) to ensure their suitability for subsequent use. Additionally, the animals are likely to need to undergo regular, detailed monitoring, not only with respect to their welfare but also to assess and ensure their suitability for use. Since all of the techniques applied to the animals are being performed for a scientific purpose Directive 86/609/EEC(39) and Convention ETS No. 123(40) should apply to the source animals as well as to those used for research purposes.
102. Pigs have been considered to be the preferred source animal for xenotransplantation and most of the detailed guidelines available for source animal husbandry and care refer to this species. However, the widening of the definition of xenotransplantation means that other species may now be used. The detailed points in the explanatory notes refer to pigs but the principles should apply to all species used.

103. Detailed guidance on the maintenance of pigs in xenotransplantation programmes has been developed in documents such as the UK Home Office's *Draft Code of Practice for the Housing and Care of Pigs used as Xenotransplant Source Animals*[^41]. These documents set out standards for all xenotransplantation programmes. Further guidance regarding the maintenance and welfare of pigs is available in the Report of the EU Scientific Veterinary Committee, 1997[^42] and in the scientific literature[^43,44].

104. It should be noted that this Article indicates that the “principles” of Appendix A of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes should be complied with. Indeed, although this European Convention foresees that there are exceptions, it may not always be possible to fully follow the provisions of this Appendix because of the requirements of biosecurity necessary for xenotransplantation.

**Article 23 – Husbandry, care, use and requirements of animals**

105. Pigs are sentient, intelligent and inquisitive animals that have retained many of the complex behavioural characteristics of their wild ancestors. These include rooting and exploratory behaviour, and social interactions within small, stable groups. They have limited thermo-regulatory ability, but their hearing and, in particular, their olfactory abilities are highly developed. Housing, husbandry and general management of pigs should take account of these needs.
106. The optimal environment depends on many factors including age, feeding regime and social circumstances. There are general guidelines in the scientific and technical literature\(^{(45,46,47,48,49)}\) but decisions regarding the adequacy of the environment on a day to day basis should be based on frequent observation by an experienced stockperson of the behaviour and physical well being of the pigs themselves.

107. Animals should be housed in facilities appropriate for the species, built and operated in line with recommendations available such as the *Guide for the Care and Use of Laboratory Animals*\(^{(50)}\) and meet regular inspection requirements, including details of source animal and health surveillance record systems.

108. To achieve satisfactory standards of welfare for pigs, the systems of accommodation, husbandry and care should ensure that the animals have:

a) company of their own kind, allowing them to live in stable groups with other familiar individuals – animals should never be held in complete isolation without visual, auditory and olfactory contact with other pigs.

b) adequate amounts of space, in both a lying area (in which all pigs should be able to lie down together in lateral recumbency) and the general ‘loafing’/dunging area, in order to allow all pigs to move around freely and be able to escape and hide from other pigs if necessary.

c) housing which protects against physical discomfort, providing a clean, dry, comfortable lying area, suitable non-abrasive, non-slip flooring, and an enclosure without sharp protrusions or other characteristics likely to cause injury.

d) adequate quantities of clean, fresh water continuously available; adequate quantities of diet formulated to satisfy the nutritional requirements of the animals and ensure good welfare. Where animals are held in groups, care should be taken to ensure that subordinate animals have adequate access to food and water to avoid potential sources of aggression.
e) a thermally comfortable environment, ensuring that the temperature remains within the pigs' thermoneutral range and avoiding lengthy exposure to low humidity.

f) an acceptable atmosphere, maintaining appropriate ventilation for the stocking densities in use; ensuring that aerial contaminants (e.g. ammonia, inhalable dust) are kept within non-aversive and non-harmful limits; and avoiding draughts.

g) appropriate lighting for a period equivalent to normal daylight hours, and providing a period of darkness – pigs should never be kept in continuous complete darkness.

h) minimum levels of continuous background noise and avoidance of unexpected loud noise since high levels of noise are potential stressors.

i) environmental enrichment, providing adequate amounts of straw or other suitable materials for manipulation, to satisfy pigs' behavioural needs in terms of rooting, recreational and investigative behaviour.

j) competent, knowledgeable stock-persons who understand the pigs' needs and behaviours, and are dedicated to promoting their well-being and preventing or minimising any fear, distress and discomfort at all times – gentle, calm human contact with the pigs is important, as this will minimise stress during handling and procedures.

k) competent, knowledgeable, veterinary care, by those with specialist experience and understanding of pig health and welfare.

Space allowances

109. Minimum pen dimensions and space allowances for individual and groups of animals are specified below. These comply with the current recommendations in the European Convention ETS No. 123\(^{(52)}\) and Directive 86/609 EEC\(^{(53)}\). Note that the shape of the pen, its complexity and contents are as important to the animal as overall size.
### Space Allowances for Weaners, Growing & Adult Pigs

<table>
<thead>
<tr>
<th>Species – Pigs</th>
<th>Minimum Floor Area – Groups (per pig)</th>
<th>Minimum Floor Area – Single Pigs</th>
<th>Minimum Feed Rack</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 10 kg</td>
<td>0.25 m²</td>
<td>1.0 m²</td>
<td>0.15 m</td>
</tr>
<tr>
<td>10 – 20 kg</td>
<td>0.5 m²</td>
<td>1.5 m²</td>
<td>0.20 m</td>
</tr>
<tr>
<td>20 – 30 kg</td>
<td>1.0 m²</td>
<td>2.0 m²</td>
<td>0.20 m</td>
</tr>
<tr>
<td>30 – 50 kg</td>
<td>1.3 m²</td>
<td>2.0 m²</td>
<td>0.25 m</td>
</tr>
<tr>
<td>50 – 100 kg</td>
<td>2.0 m²</td>
<td>3.0 m²</td>
<td>0.30 m</td>
</tr>
<tr>
<td>100 – 150 kg</td>
<td>2.7 m²</td>
<td>4.0 m²</td>
<td>0.35 m</td>
</tr>
<tr>
<td>Over 150 kg</td>
<td>3.75 m²</td>
<td>5.0 m²</td>
<td>0.40 m</td>
</tr>
<tr>
<td>Adult Boars</td>
<td>–</td>
<td>7.5 m²</td>
<td>0.50 m</td>
</tr>
</tbody>
</table>

Service pens should have a minimum floor area of 10.5 m², to allow a sufficient area for mating.

**Breeding animals**

**Sows**

110. The design of the farrowing area should be appropriate for the size of the sow, to allow the animal to lie down comfortably, to stand upright and to expose all teats to the piglets. The sow should be provided with a solid floored lying area, at least equal to 75% of the overall area and some form of nesting material should be provided, especially as farrowing approaches.

111. The accommodation where sows and piglets are kept should enable the fulfilment of the special behaviour patterns of the sow before and after parturition, and those of the piglets after birth. Thus even though the use of farrowing crates can safeguard piglets’ survival and welfare under some conditions, the close confinement of sows during the perinatal and suckling periods should be limited as far as possible and loose housing systems should be preferred. Farrowing crates significantly limit the behavioural repertoire of the sow and therefore the sow should
be given greater freedom in later lactation when piglet viability is well established. From five days after farrowing, sows should have at least enough space to turn around easily and the more welfare friendly systems which allow this should be promptly adopted.

112. The period of confinement should be minimised, with animals crated no more than 5 days pre-farrowing, and returned to an extensive group housing system at weaning, generally by 4 weeks post-partum, or earlier if early weaning practices (segregated/medicated early weaning) are considered necessary and are used.

Boars

113. Adult boars are commonly housed singly. However, animals raised together from an early age have been maintained successfully in pairs as adults. Group housing is therefore encouraged, provided that social harmony can be maintained. If single housing is unavoidable then auditory and olfactory stimuli with other pigs should be available at all times, with the opportunity for visual and safe tactile contacts.

114. Boars tend to be physically segregated for long periods; therefore particular care should be taken to provide an enriched environment that addresses their behavioural needs.

Additional animal requirements

115. Young animals should be weaned into social groups. Siblings from one litter should not be separated unnecessarily.

116. Some types of biocontainment facilities are totally inappropriate for some species. For example, pigs should not be wholly reared in gnotobiotic conditions and should not be reared beyond the age of four weeks in an isolator.

117. Pigs living within a barriered animal unit are totally dependent on humans for their health and well being. The physical and psychological state of the animals will be influenced by their surroundings, food, water and the nature and quality of the care and attention provided by the animal house staff.
118. Restricted environments can lead to behavioural and physiological abnormalities. Adequate complexity is required within the basic pen design to allow the animal to carry out a range of normal behaviours. For example, visual barriers can be useful to allow the pigs to control social interactions and provide refuges. In extensive systems, pigs spend many hours exploring their environment, using their highly sensitive snout to root; laboratory housed pigs have little opportunity to express this sort of behaviour. In the absence of suitable foraging substrate and when there is insufficient diet to maintain satiety, abnormal stereotypic behaviours, such as bar chewing, and increased aggression can develop. Material, such as straw, can provide for many of these behavioural requirements, and should be provided where possible. If such material cannot be provided because of the nature of the barrier system, then alternative enrichment strategies should be included e.g. food balls; other ‘toys’; pebble trays; chains; scratching posts; showers.

119. Where pigs develop stereotypes or abnormal behaviours that injure other animals (e.g. tail, ear or vulva biting) additional enrichment to encourage foraging/rooting should be provided as a matter of urgency and an appropriate enrichment programme developed and implemented. If necessary, animals may need to be removed from the group.

120. Castration, tooth clipping or grinding, and tail docking should not be necessary for pigs produced for xenotransplantation programmes. They should only be carried out to deal with specific welfare problems by specially trained and competent persons using appropriate equipment. If these do arise then the cause should be examined and if resulting from the husbandry system this should be adjusted to avoid repetition.

Training of Staff

121. Appropriate training of staff is essential to ensure that high standards of pig husbandry and care are provided, and that barrier security can be maintained. The importance of such training was recognised by the Multilateral Consultation of parties to
Convention (ETS No. 123)(55). Attendance on a course satisfying the requirements of the appropriate Federation of European Animal Science Associations (FELASA) training category should be strongly recommended.

122. Training should include an introduction to the natural history and behaviour of the pig, which will illustrate their needs in a captive breeding system. Animal care staff should be trained to recognise normal behaviour, in order that any abnormalities can be identified at an early stage. Pig husbandry, care and welfare, principles of barrier production and maintenance, barrier hygiene, internal management practices, breeding and health record keeping practices should also be included.

**Article 24 – Responsibility for husbandry and care of animals**

123. Records should be kept of the numbers of animals used in both xenotransplantation and pre-clinical procedures.

**Article 25 – Surgical derivation and early weaning techniques**

124. Records should be kept of all surgical derivation and segregated/medicated early weaning procedures and any associated welfare problems. Such records should be subject to regular review.

**Article 26 – Transport of animals**

125. All transport should be carried out in strict compliance with EU and other international legislation (the *European Convention for the Protection of Animals During International Transport* currently being revised; *Draft Code of Conduct for the International Transport by Road of cattle, sheep, goats, pigs, horses, poultry, deer, reindeer, rabbits and ostriches*). Detailed guidance specifically on transport of pigs is provided in the *Draft Code of Practice* published by the UK Home Office.
126. Only animals in good health should be transported. The time in transit should be kept to a minimum. Stress should be minimised by making animals as comfortable as possible in their pens or containers with due regard to conditions likely to prevail throughout the journey. Animals that are incompatible should not be transported together.

127. There is evidence that pigs may become travel sick (59) so withdrawal of food for four hours prior to transportation is recommended, although free access to water (and milk in the case of pre-weaned piglets) should be provided at all times. It should be noted, moreover, that since pigs should not be denied food for long periods, journeys should not be prolonged.

128. Pregnant animals should not be transported during the first six weeks of pregnancy, and particularly not within the last 11 days of the expected birth and the 48 hours thereafter (see draft European Transport Convention (60)). Special consideration should be given to the welfare of young piglets during transport, in particular with regard to the maintenance of suitable environmental controls and arrangements for feeding and watering.

129. Emergency plans should be in place to deal with possible problems during transport, such as vehicle breakdown.

130. Those in charge of pigs during transport should be trained with the necessary skills. Moreover they should be knowledgeable of the behaviour and physical needs of pigs. Drivers should be trained in such a way as to minimise risk of injury or stress to the animals.

**Article 27 – Organ and tissue procurement from animals**

131. Where surgery is to be performed, suitable operating facilities should be provided, including separate preparation areas for the animals, equipment and staff. General veterinary treatment rooms should also be provided.
132. Surgery and killing of animals should not be performed in rooms where animals are normally housed, unless in the case of the emergency killing of a badly injured animal, welfare may be further compromised by moving the animal.

133. To avoid animal suffering, the sequential harvest of solid organs from individual animals in xenotransplantation should not be permitted unless this is performed under a single general anaesthetic from which the source animal does not recover consciousness.

134. The procurement of tissues and cells from individual animals during xenotransplantation research should be undertaken in conformity with Article 11 of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (ETS No. 123), which states:

1. **At the end of the procedure it shall be decided whether the animal shall be kept alive or killed by a humane method. An animal shall not be kept alive if, even though it has been restored to normal health in all other respects, it is likely to remain in lasting pain or distress.**

2. **The decision referred to in paragraph 1 of this Article shall be taken by a competent person, in particular a veterinarian, or the person who, in accordance with Article 13, is responsible for, or has performed, the procedure.**

3. **Where, at the end of the procedure:**
   a. **an animal is to be kept alive, it shall receive the care appropriate to its state of health, be placed under the supervision of a veterinarian or other competent person and kept under conditions conforming to the requirements of Article 5. The conditions laid down in this sub paragraph may, however, be waived where, in the opinion of a veterinarian, the animal would not suffer as a consequence of such exemption;**
b. an animal is not to be kept alive or cannot benefit from the provisions of Article 5 for its well being, it shall be killed by a humane method as soon as possible.

4. No animal which has been used in a procedure entailing severe or enduring pain or suffering, irrespective of whether anaesthesia or analgesia was employed, shall be used in a further procedure unless it has returned to good health and well being and either:

a. the further procedure is one in which the animal is subject throughout to general anaesthesia which is to be maintained until the animal is killed; or

b. the further procedure will involve minor interventions only.

Article 28 – Collection of animal records

135. Biological samples and records from the source animal should be systematically archived. Archived items should include all the source animal’s necropsy reports together with stored serum and plasma, viable leukocytes and samples of xenotransplant cells and tissues in addition to other major organs (spleen, liver, kidney, heart, bone marrow, gut, central nervous system).

136. If genetically modified animals are used, recording of any unusual or unexpected traits such as abnormal phenotypes or behaviour is very important in order to monitor the effects of the genetic modification which may not become apparent until at least the second generation. If abnormal traits are detected then additional justification for the use of these animals for xenotransplantation may be required.

Article 29 – Pre-clinical research

137. Since the European Convention and the European Council Directive addressing the protection of animals used for experimental and other scientific purposes mentioned in Article 22 may not be applicable in some member states, and in
order to protect animals used in pre-clinical research, Article 29 of the Recommendation extends the protection provided by Articles 22-28 to all animals used in pre-clinical research. This is in addition to providing husbandry and care appropriate to the needs of animals and ensuring that any experimental technique is carried out in a humane manner. This includes following current international laboratory animal science principles such as seeking replacements for animals, reducing the numbers used and the refinement of interventions.
Chapter VI

Provisions relating to the ethical, social and psychological acceptability of xenotransplantation

Article 30 – Public debate

138. Because of the novelty of xenotransplantation and the potential risks involved both for the individual and the community, public information is crucial. This is especially the case since clinical xenotransplantation research using tissues and cells is already underway and the results of such activities in addition to any further clinical work should be carefully and fully monitored and reported. This will help scientists, legislators and the general public understand both what is involved in xenotransplantation and the consequences and implications of such a procedure. Indeed the information will provide the necessary framework for the development and application of licensing, monitoring and the surveillance of future xenotransplantations.

139. It is vital that all results – both negative and positive should be accurately reported and fully accessible both to the general public and to those who carry responsibility for the regulation and
Recommendations of the Committee of Ministers to member states

control of xenotransplantation. Negative results and consequences carry considerable weight in any assessment of further work and development of xenotransplantation technology.

140. Assessing the public’s reaction, concern, approval or disapproval of xenotransplantation will require careful presentation through the various media of all information about xenotransplantation research and raises questions about how public debate on such issues is conducted and public opinion assessed.

141. The fact that certain xenotransplantation activities begun before any public information was provided does not mean that it is pointless to provide such information.
Chapter VII

Co-operation between parties

Article 31 – International co-operation in medical research

142. This Article indicates that member states should take appropriate steps to facilitate the co-ordination of research in xenotransplantation. This is important in order to improve the efficacy and safety of xenotransplantation, to avoid unnecessary duplication and to minimise animal use and suffering.

143. It is important that commercial concerns relating to xenotransplantation are included at the very beginning of the international co-operation and collaboration process so that their views and suggestions can be included in the discussions.

Article 32 – International co-operation in public health

144. In order to ensure that member states communicate without delay to national public health authorities of member states and other concerned states of any events, in particular of infection, possibly related to a xenotransplantation, all relevant information should be centralised at a national level. It would be desirable that an
international registry of xenotransplantation together with an international data communication procedure is established to ensure that timely measures are taken to protect public health.

145. International co-operation and collaboration should also encourage different countries engaged in xenotransplantation to prepare a uniform set of guidelines. This should be undertaken both because international conventions require that states do not put their neighbours at risk and because much benefit may be obtained in sharing the experience arising from national deliberations regarding medical safety, research and clinical work.
Chapter VIII

Compensation for undue damage

Article 33 – Compensation for undue damage

146. This Article applies to the xenotransplantation field the general principle already contained in the Convention on Human Rights and Biomedicine (ETS No. 164), that any person who has suffered undue damage resulting from an intervention is entitled to fair compensation. The Convention uses the expression “undue damage” because in medicine some damage, such as amputation, is inherent in the therapeutic intervention itself.

147. The due or undue nature of the damage will have to be determined in the light of the circumstances of each case. The cause of the damage might take the form of either an act or an omission. In order to give entitlement to compensation, the damage must result from the xenotransplantation.

148. Compensation conditions and procedures are prescribed by national law. In many cases, this establishes a system of individual liability based either on fault or on the notion of risk or strict liability. In other cases, the law may provide for a collective system of compensation irrespective of individual liability.

149. On the subject of fair compensation, reference can be made to Article 50 of the European Convention on Human Rights, which allows the Court to afford just satisfaction to the injured party.
Chapter IX

Reports on the implementation of the recommendation

Article 34 – Implementation of the Recommendation

150. Because of the possible new developments in xenotransplantation, guidelines in the form of recommendations were considered as being more appropriate to regulate this field than a Convention, whose entry into force usually takes a number of years. Accordingly, the present guidelines are in the form of an official Recommendation from the Committee of Ministers of the Council of Europe to all member states; they are also communicated to the non-member states who have participated in the drafting of this document. The Secretary General of the Council of Europe can ask any member state to provide an explanation on the manner in which its internal law ensures the effective implementation of any of the provisions of this Recommendation, of any xenotransplantation activity and on any adverse event as referred to in Article 9.
Summary of the discussions with the representatives of the European Court of Human Rights concerning legal issues relevant to xenotransplantation

The representatives of the European Court of Human Rights introduced the Convention for the Protection of Human Rights and Fundamental Freedoms of the Council of Europe by explaining that it should be understood as a legal instrument aimed at securing individual rights and as such it may be of limited relevance to policy issues in the field of bioethics. Many of the rights in the Convention were subject to permissible restrictions and involved establishing a proper balance between competing interests.

In determining whether a restriction or “interference” is in conformity with the requirements of the Convention, the Court examines whether it has a proper legal basis, and in particular whether the law is accessible and the effect of its application is foreseeable, and whether the interference can be regarded as justified in a democratic society in pursuit of one of the legitimate aims specified in the Convention.

In the context of xenotransplantation, this implied the need for a clear legal basis for obtaining informed consent and for providing an adequate explanation of the related risks.

The Convention did make provision for the compulsory confinement of individuals but only in specific cases, an exhaustive list of which was given in the Convention. In addition, detention had to be
both “lawful” and “in accordance with a procedure prescribed by law” and the Convention added a variety of safeguards against arbitrary deprivations of liberty. More specifically, the Convention in Article 5 (1) (d) permitted the lawful detention of persons to limit the spreading of infectious diseases.

With regard to Article 8 of the Convention, which protects the right to respect for, *inter alia*, private and family life, it was explained that interferences could be justified provided they were necessary in a democratic society. Moreover, in certain circumstances it might be considered that an individual, by giving consent to a particular interference, had waived his or her rights.

The representatives of the European Court of Human Rights concluded that the Convention did not address any rights to a treatment of a patient, as such, but might be relevant to the question whether a state had the appropriate legal framework and procedures in place to resolve any possible conflicts between actors. Furthermore, with specific regards to xenotransplantation, very little jurisprudence of any relevance could be found in the case-law of the Convention during the last 40 years.
Notes

1. A more detailed discussion of these concerns can be found in the state of the art report on xenotransplantation drafted by the Working Party (CDBI/CDSP-XENO).


9. The World Medical Association’s Declaration of Helsinki and its subsequent revisions could be consulted in this regard. World Medical Association Declaration of Helsinki: Ethical Principles for Medical research involving human subjects. Adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975, the 35th WMA General Assembly, Venice, Italy, October 1983, the 41st WMA General Assembly, Hong Kong, September 1989, the 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996, and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000.


22. The Swedish Committee on Xenotransplantation in their 1999 report stated that: “The Committee considers it unacceptable to use non-human primates as source animals, both for ethical and animal protection reasons and also having regard to the risk of infection. However, non-human primates may be, to a limited extent, used as recipient animals during the pre-clinical research phase.” Swedish Committee on Xenotransplantation: From one species to another – transplantation from animals to humans. Swedish Government Official Report No. 1999:120, 1999.


50. Guide for the Care and Use of Laboratory Animals, NIH publication No. 86-23, revised 1985.


Recommendations of the Committee of Ministers to member states

of Member States regarding the protection of animals used for experimental and other scientific purposes.


55. Multilateral Consultation of parties to Convention ETS No. 123 (see Resolution on education and training of persons working with laboratory animals adopted by the Multilateral Consultation, 3 December 1993).

56. The European Convention for the Protection of Animals During International Transport currently being revised.

57. Draft Code of Conduct for the International Transport by Road of cattle, sheep, goats, pigs, horses, poultry, deer, reindeer, rabbits and ostriches.


60. The European Convention for the Protection of Animals During International Transport currently being revised.
Preamble

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve a greater unity between its members;


Having regard to the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes;
Recommendations of the Committee of Ministers to member states

Having regard to the Resolution of the Committee of Ministers (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, the Final Text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987) and the Recommendation R (97) 15 of the Committee of Ministers to member states on xenotransplantation;

Bearing in mind Recommendation 1399 (1999) of the Parliamentary Assembly on xenotransplantation;

Bearing in mind recent reports from the OECD, the WHO and other national and international organisations;

Taking into account the shortage of organs and tissues of human origin available for transplantation;

Considering that xenotransplantation might be one of the possible therapeutic responses to this shortage;

Noting that xenotransplantation remains largely an experimental activity and that research is essential for the achievement of progress in this field;

Aware of the risks of rejection and illness xenotransplantation may cause in the recipient patient;

Mindful of the considerable risks which might arise from xenotransplantation in the field of public health and the transmission of diseases;

Considering that it is the responsibility of each member state to adopt adequate measures in order to address them and conscious that in some countries no appropriate regulations exist;

Considering that public health concerns require common provisions applicable in all the member states of the Council of Europe in which xenotransplantation is envisaged;

Considering that worldwide cooperation between states in this field is necessary;
Recommendations of the Committee of Ministers to member states

Considering that no clinical xenotransplantation research should take place unless sufficient efficacy and safety is demonstrated through pre-clinical research;

Conscious that the need for such a demonstration will considerably limit the number of xenotransplantations in the coming years, thus allowing for an appropriate risk assessment;

Considering that xenotransplantation of cells and tissues is already being carried out in a number of states and that stringent regulations are thus urgently required;

Mindful of the social, ethical, cultural, legal and psychological problems which might be associated with xenotransplantation;

Mindful of the ethical and welfare issues associated with the use of animals for xenotransplantation and the associated research;

Noting the public concern over the issues related to xenotransplantation and stressing the importance of undertaking a public debate on this subject,

A. Recommends that the governments of member states:

- take the necessary measures to put their legislation and practice in the field of xenotransplantation in conformity with the following principles and guidelines with a view to minimising the risk of transmission of known or unknown diseases and infections to populations;
- co-operate in the setting-up of world-wide surveillance procedures and agreements;
- ensure a wide dissemination of this recommendation, in particular among all persons, organisations and bodies, public or private, responsible for organising and carrying out xenotransplantation;
- take steps to make the provisions of this recommendation subject to public debate.
B. Decides that this recommendation will be re-examined at appropriate intervals and not later than in three years’ time.

C. Instructs the Secretary General to bring the contents of this recommendation to the attention of the non-member states and international organisations which have participated in its preparation and to invite them to participate in the setting-up of an international surveillance network.

GUIDELINES

Chapter I – Object, scope and definitions

Article 1 – Object of the recommendation

This recommendation aims:

- to protect, in both the short and long term, public health, patients, their close personal contacts and the professional staff involved in xenotransplantation, and
- to provide adequate protection for the animals used in xenotransplantation.

Article 2 – Scope of the recommendation

This recommendation covers all xenotransplantation activities involving human beings as recipients.

Article 3 – Definition

For the purpose of this recommendation, xenotransplantation is defined as any procedure that involves the transplantation or infusion into a human recipient of:

- live animal cells, tissues or organs, or
- human body fluids, cells, tissues or organs that have had ex vivo contact with live animal cells, tissues or organs.
Chapter II – General provisions

Article 4 – Xenotransplantation – the setting

No xenotransplantation should be carried out in a member state that does not provide regulation for xenotransplantation activities in conformity with the provisions of this recommendation.

Article 5 – Xenotransplantation authorisation

No xenotransplantation activity should be carried out in a member state unless authorisation is given by a body officially recognised as competent for this purpose, in accordance with the provisions contained in the following two paragraphs:

1. Authorisation for clinical xenotransplantation research should only be given if:
   a. pre-clinical research has demonstrated, in accordance with internationally accepted scientific standards, that:
      i. in the light of current scientific knowledge it is highly probable that there is no risk, in particular of infection, for public health;
      ii. the potential level of efficacy and safety for the patient may justify the intervention having regard to the risks incurred;
   b. all substantive and procedural conditions generally applicable to clinical research are fulfilled.

2. Xenotransplantation should not be authorised other than in clinical research unless, on the basis of clinical data:
   i. there is adequate evidence, in accordance with internationally accepted scientific standards, that no risks, in particular of infection, to the general population exist, and
   ii. the therapeutic benefit of the xenotransplantation has been established.
Article 6 – Xenotransplantation teams and centres

No xenotransplantation should be carried out unless it is undertaken by an accredited team in an authorised centre.

a. The teams carrying out the xenotransplantation should be appropriately qualified and comprise all the necessary scientific and medical expertise.

b. The centres should have received an authorisation by the competent bodies prior to beginning the xenotransplantation.

Chapter III – Protection of Public Health

Article 7 – Public Health protection plan

Member states should have a plan in place to address any events, in particular of infection, possibly related to a xenotransplantation which could compromise public health.

In particular, public authorities should take appropriate measures, in conformity with the principles of necessity and proportionality, to respond to events of transmissible or previously unknown illness related to xenotransplantation. These measures, if exceptional circumstances so require, might include isolation.

Article 8 – Collection and storage of biological samples and information

Information and biological samples concerning the source animals used in xenotransplantation and the recipients should be collected and stored in order to ensure traceability and long-term monitoring.

Article 9 – Follow-up

1. All protocols for clinical research should be accompanied by a plan to ensure the traceability and monitoring of the recipients, their close personal contacts and the professional staff involved in xenotransplantation in order to detect and deal with any
adverse events, in particular of infection, possibly related to xenotransplantation.

The plan should include communication without delay to the competent body at national level of any such events.

2. Any xenotransplantation other than in clinical research should be accompanied by a plan to:
   – ensure the traceability of the recipient as well as, depending on the circumstances, of other persons mentioned in paragraph 1;
   – monitor, wherever necessary, the persons mentioned in paragraph 1.

The plan should include communication without delay to national public health authorities of any events, in particular of infection, possibly related to xenotransplantation and which could be of relevance to public health.

Article 10 – Precautions relating to the transmission of disease

All appropriate measures, in accordance with internationally recognised criteria, should be taken to prevent the risk of transmission of infectious agents from source animals.

Only animals bred specifically for xenotransplantation should be used. An appropriate Quality Assurance system encompassing all the stages from the production of the source animals to the final collection of the xenotransplants should be set up.

Article 11 – Prohibition relating to the use of non-human primates

1. Non-human primates should not be used as source animals for xenotransplantation.

2. Exceptionally, authorisation for the xenotransplantation of cell lines obtained from non-human primates may be given if:
   – the conditions under Article 5 are fulfilled, and
   – specific protective measures for these animals have been addressed. This implies that Great Apes should not be used as source animals in xenotransplantation.
Chapter IV – Protection of patients and close personal contacts

Article 12 – Conditions for patient participation

No xenotransplantation should be carried out unless the following specific conditions are fulfilled:

i. There is no other appropriate therapeutic method of comparable effectiveness available for the patient.

ii. The data resulting from pre-clinical research suggest or, where appropriate, the data resulting from prior clinical research indicate a clear therapeutic benefit for the xenotransplantation patient. In particular these data should:
   – have demonstrated an adequate function of the xenotransplant in relevant models for an appropriate period of time through a clinically applicable methodology,
   – provide sufficient reasons to believe that rejection can be overcome and that the xenotransplant can function adequately in humans.

iii. The risks which may be incurred by the patient are not disproportionate to the potential therapeutic benefit of the procedure.

In particular, the evaluation through pre-clinical research of the risks for adverse events and transmission of infectious agents to the recipient, as based on international standards for laboratory results and diagnostic assays, should have demonstrated sufficient safety.

Article 13 – Information to be given to patients

1. Patients participating in a xenotransplantation should be adequately informed in a comprehensible manner of the nature, objectives, possible benefits, potential risks and consequences of the procedure, as well as of any constraints that may be linked to it.

2. In particular patients should also be made aware of the constraints of monitoring and precautionary measures that may become
necessary subsequent to xenotransplantation. Such measures will, according to the principles of necessity and proportionality, be adapted to the circumstances and adjusted in accordance with the assessment, based on current scientific and medical knowledge, of the risks generated by each of the procedures involved, and may in particular include:

a. the collection of personal data and inclusion in a register;

b. the provision by the medical team, in accordance with Article 14, of information concerning the risks of infection and the constraints associated thereto;

c. long-term medical monitoring including repeated biological samples being taken and archived;

d. reporting any significant unexplained symptoms or illness that may arise after the xenotransplantation;

e. maintaining contact with the medical team;

f. taking precautions with respect to sexual activity;

3. Patients should be informed that, in accordance with Article 21, constraints mentioned hereinabove may be imposed if the person concerned refuses to comply with them.

Article 14 – Information to be given to close personal contacts of the patient

To protect close personal contacts and warn of the possible risks they might pose to the general public, the patient’s close personal contacts should, with his or her consent, be informed by the medical team of the
patient’s envisaged participation in a xenotransplantation, of the risks of infection and of the consequences for them of such participation, and in particular, of the constraints which may be applicable.

The patient should also ensure that such information is provided to any future close personal contacts.

Article 15 – Information to be given to the professional staff involved in xenotransplantation

Professional staff involved in xenotransplantation should be fully aware of the risks of infection as well as the possible consequences and constraints which may derive from their participation in xenotransplantation.

Article 16 – Consent to xenotransplantation

1. No xenotransplantation should be carried out without:
   i. the documented, specific, free and informed consent of the patient to the procedure and any necessary specific constraints; and
   ii. the provision by the patient to the medical team of the necessary information concerning his or her current close personal contacts and the acceptance by the patient that his or her current and future close personal contacts be given information in accordance with Article 14.

2. Prior to xenotransplantation, the consent to carry out the intervention may be freely withdrawn at any time.

Article 17 – Counselling and support

The patients and their close personal contacts should be given proper information and have access to counselling and support by experts outside the team both before and after the xenotransplantation. This informing and counselling process should include the biomedical, ethical, psychological and social aspects of xenotransplantation.
Recommendations of the Committee of Ministers to member states

**Article 18 – Right to medical care**

A refusal to participate, or a withdrawal of consent prior to the xenotransplantation, should not prejudice the patient’s right to receive all other appropriate medical care in due course. The patient’s consent to participate in a xenotransplantation should not prejudice his or her right to benefit from an allotransplant that becomes available while awaiting xenotransplantation, if medically indicated.

**Article 19 – Patients not able to consent**

1. Where xenotransplantation has been authorised for use other than in clinical research according to Article 5 paragraph 2, it may be carried out on a person not able to consent only if the following conditions are fulfilled:

   - there is no therapeutic alternative of comparable effectiveness available to the patient,
   - taking into account the constraints and conditions to which the person will or may be subjected according to Articles 13 and 14, the intervention is expected to result in a direct and important benefit for the patient, and
   - the representative or an authority or a person or body provided for by law, after receiving the information referred to in Article 13, has authorised both the intervention and the provision of the necessary information to the present and future close personal contacts of the patient.

2. Patients unable to consent should not undergo clinical xenotransplantation research as referred to in Article 5, paragraph 1.

   Exceptionally, a patient unable to consent may participate in a clinical xenotransplantation research intervention if the following specific conditions are fulfilled:

   - there is adequate indication, on the basis of prior clinical research, that the xenotransplantation might be lifesaving,
– there is no alternative means of saving the life of the patient,
– taking into account the constraints and conditions to which the person will or may be subjected according to Articles 13 and 14, the intervention is expected to result in a direct and important benefit for the patient, and
– the representative or an authority or a person or body provided for by law, after receiving the information referred to in Article 13, has authorised both the patient’s participation in the clinical xenotransplantation research and the provision of the necessary information to the present and future close personal contacts of the patient.

Article 20 – Confidentiality

All personal data relating to the recipient person and, where such data exist, their close personal contacts should be considered to be confidential.

Without prejudice to the provision of Article 8, such data should be collected, processed and communicated according to the rules relating to professional confidentiality and personal data protection.

Article 21 – Compulsory constraints

If, after the xenotransplantation has been carried out, the recipient or his or her close personal contacts refuse to comply with the constraints associated with xenotransplantation, public authorities should intervene and take appropriate measures, where public health protection so requires, in conformity with principles of necessity and proportionality.

Depending on the circumstances and in accordance with the procedures provided for by national law, such measures might include registration, compulsory medical follow-up and sampling.
Chapter V – Protection of animals

Article 22 – Compliance with animal protection regulations
All animal use in xenotransplantation should comply with the provisions of the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes including the principles of Appendix A and Council Directive 86/609/EEC on the approximation of laws, regulations and administrative provisions of member states regarding the protection of animals used for experimental and other scientific purposes including Annex II.

These provisions should apply to source animals in addition to their sires and dams in source production units, pre-transplantation holding facilities, tissue harvest areas and during transport.

Article 23 – Husbandry, care, use and requirements of animals
The husbandry and care for all animals used in xenotransplantation should take account of their physiological, social and behavioural needs and should be designed to ensure their well being, particularly where breeding animals are maintained for long periods. The pain, suffering or distress and the number of animals used should be minimised.

Article 24 – Responsibility for husbandry and care of animals
There should be clearly assigned and documented responsibilities for husbandry and care of the animals used in xenotransplantation from birth to death, with a sufficient number of appropriately trained and competent staff available to inspect and care for them.

Article 25 – Surgical derivation and early weaning techniques
Surgical derivation and segregated/medicated early weaning production techniques should only be used where essential to produce animals of appropriate health status for use in xenotransplantation.
Recommendations of the Committee of Ministers to member states

Article 26 – Transport of animals
Transport of animals for xenotransplantation should be kept to a minimum. If transportation is necessary, adequate arrangements should be made for the dispatch, receipt, acclimatisation and quarantine of animals in order to minimise the associated stress. The relevant national and international legislation/regulations (including European Union Directive 95/29/EEC modifying Directive 91/628/EEC on the protection of animals during transport, and the European Convention for the Protection of Animals During International Transport (revised)) should be complied with.

Article 27 – Organ and tissue procurement from animals
Analgesia or anaesthesia should be used for the procurement of organs, tissues and cells for xenotransplantation, where it is necessary to minimise pain, suffering and distress of the animals.

If, as a result of the procurement, the subsequent health and welfare of the animals would be compromised, the animals should be killed by an appropriate method.

Sequential harvest of solid organs from individual animals should not be permitted.

Article 28 – Collection of animal records
Detailed records should be maintained of the derivation, source, use and final disposal of all animals bred for or used in xenotransplantation. Any unusual or unexpected traits or events should be recorded.

Article 29 – Pre-clinical research
The provisions of Articles 22 to 28 should also apply to animals used in pre-clinical research carried out to support clinical xenotransplantation research.
Chapter VI – Provisions relating to the ethical, social and psychological acceptability of xenotransplantation

Article 30 – Public debate

In accordance with the principles stated in Article 28 of the Convention on Human Rights and Biomedicine, member states should take active steps to ensure that the fundamental questions raised by xenotransplantation are the subject of appropriate public discussion particularly in light of relevant medical, psychological, cultural, ethical, legal, social and economic implications.

Chapter VII – Co-operation between parties

Article 31 – International co-operation in medical research

Member states should co-operate through international surveillance procedures and agreements. They should also take appropriate steps to facilitate the co-ordination of research in xenotransplantation in order to improve its efficacy and safety, to avoid unnecessary duplication and to minimise animal use and suffering.

Article 32 – International co-operation in public health

Every member state should communicate without delay to national public health authorities of other member states and other concerned states any events, in particular of infection, possibly related to a xenotransplantation which could compromise public health.

Chapter VIII – Compensation for undue damage

Article 33–Compensation for undue damage

The person who has suffered undue damage resulting from a xenotransplantation is entitled to fair compensation according to the conditions and procedures prescribed by law.
Chapter IX – Reports on the implementation of the recommendation

Article 34 – Implementation of the recommendation

On receipt of a request from the Secretary General of the Council of Europe any member state should furnish an explanation on the manner in which its legislation and practice in the field of xenotransplantation integrate the principles and guidelines of this recommendation, on any xenotransplantation activity and on any adverse event as referred to in Article 9.
Recommendation Rec(2003)12 of the Committee of Ministers to member states on organ donor registers

(Adopted by the Committee of Ministers on 19 June 2003 at the 844th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common regulations in the health field;

Having regard to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (the Convention on Human Rights and Biomedicine) (ETS No. 164);

Having regard to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning the Transplantation of Organs and Tissues of Human Origin (ETS No. 186);
Bearing in mind that:

- the Protocol concerning the Transplantation of Organ and Tissues of Human Origin requires member states to have a legally recognised system specifying the conditions under which removal of organs or tissues is authorised;
- by virtue of Article 8 of the said protocol, member states should take appropriate measures to inform the public, namely about matters relating to consent or authorisation with regard to the removal of organs or tissues from deceased persons;
- Article 17 of the said protocol prohibits the removal of any organ or tissue unless the consent or authorisation required by national law has been obtained by the person proposing to remove the organ or tissue;

Recalling the general principles relating to data protection of the Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data (ETS No. 108),

Recommends to governments of member states to conform with the principles contained in the appendix to this recommendation as regards organ donor registries:

Appendix to Recommendation Rec(2003)12

1. Careful consideration should be given to the need for, and purpose of, an organ donor register.

2. In those member states with a legal framework for organ donation which assumes people are willing to donate their organs or tissues unless they have registered their refusal (opt-out system), states must provide an effective means for people to register their decision. A national register can be an effective means of recording such decisions.
3. For member states in which consent to donation is actively sought from the donor and/or those close to them prior to organ donation (opt-in system), an organ donor register may also fulfil important functions:
   - as a means of registering the wishes of people willing to donate their organs;
   - as a means of improving the efficiency of the organ and tissue donation process by making those wishes available rapidly after the death of a potential donor has been confirmed;
   - as a means of publicising organ donation, and of involving people and organisations in realising the benefits of organ donations for themselves and for others in society;

4. Consideration should be given to the primary function of the organ donor register. Organ donor registers may:
   - be opt-out only;
   - be opt-in only;
   - register both choices, or even a third choice, such as “ask my relatives”;
   - allow simply a general agreement to donate organs and/or tissues;
   - allow wishes about the donation of particular organs and/or tissues to be specified;
   - allow registration of wishes with respect to other sensitive procedures, such as post-mortem examinations or the donation of organs/tissue for medical research.

5. Organ donor registers should ensure, that:
   - people wishing to register their wishes can do so easily and reliably;
   - people can, if they wish, specify organs and tissues they do/do not wish to donate;
   - people can revoke their entry at any time;
   - all information on people who die is removed from the organ donor registry.
6. If the organ donor register is intended to facilitate organ donation it must:
   – have details of a high proportion of potential donors/non-donors. If enquiries about potential donors give no results, health professionals will consider it a waste of time trying to access the register;
   – enable easy and rapid twenty-four hour access by health professionals needing information about a potential donor.

7. Careful consideration should be given to the costs and benefits of setting up and maintaining an organ donor register:
   – member states operating an opt-out system should, as a minimum, have a central register for those who do not wish to donate organs or tissues or any particular organ or tissue;
   – a centrally-run information technology-based organ donor register offers the greatest flexibility in terms of content, updating and rapidity of access, but data security has to be ensured;
   – everyone should be able to register their wishes;
   – registration must be easy, preferably by both written and/or electronic means;
   – written confirmation should be sent to all who register;
   – people should have a simple means of checking and amending their entry;
   – specified healthcare professionals such as intensive care staff and/or transplant co-ordinators must have twenty-four-hours-a-day access to check the wishes of potential donors by phone, fax or electronically. Such checks should normally be made only after the death of a potential donor;
   – checking the register could be made mandatory as a condition of donation.
8. Member states with organ donor registers should consider whether their register is designed and operated in a way which best meets the needs of their population and transplant service. Those member states which have an organ donor register are advised to consider the purposes and the likely advantages and disadvantages before establishing a new organ donor register.
Council of Europe
Committee of Ministers

Recommendation Rec(2004)7 of the Committee of Ministers to member states on organ trafficking

(Adopted by the Committee of Ministers on 19 May 2004 at the 884th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common action in the field of health;

Taking into account Resolution (78) 29 on harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances and the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987), and the World Health Organisation Resolution WHA 42.5 condemning the purchase and sale of organs of human origin;
Recommendations of the Committee of Ministers to member states

Having regard to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (ETS No. 164) and in particular to Articles 19 and 20 thereof;

Bearing in mind the requirements of the Additional Protocol to the above convention on Transplantation of Organs and Tissues of Human Origin, and in particular that Article 22 requires the prohibition of organ and tissue trafficking; that Article 3 requires member states to have a transplant system in place which allocates organs, and where appropriate tissues, only to those on the official waiting list; that Article 26 requires member states to provide for appropriate sanctions to be applied in the event of any infringement of the provisions contained in the aforementioned protocol; that Article 21 requires that the human body and its parts shall not, as such, give rise to financial gain or comparable advantage,

Considering that:

The universal shortage of organs and tissues can lead patients to a desperate search for a transplant which may involve unacceptable practices from a legal or ethical point of view;

Organ shortage can also encourage illegal organisations to traffic human beings for the purpose of organ transplantation, or to traffic organs obtained as a result of inducement or coercion;

Organ trafficking may undermine public confidence in organ and tissue transplantation services, decreasing the public’s disposition to legitimate organ donation, thereby exacerbating the shortage of organs and tissues for transplantation,

Recommends that the governments of member states conform with the requirements set out in the appendix to this recommendation.
Appendix to Recommendation Rec(2004)7

Article 1 – Object

Member states should protect the dignity and identity of all persons and guarantee without discrimination their fundamental rights and freedoms with regard to organ and tissue transplantation.

Member states should make it clear to all that organ trafficking exploits human beings and is illegal, and should take all possible measures to prevent organ trafficking (see Article 4).

Article 2 – Scope and definitions

1. The provisions of this recommendation shall apply to all living persons and to the removal of organs, tissues and cells from those recently deceased.

2. The provisions of this recommendation applicable to tissues shall apply also to cells, including haematopoietic stem cells.

3. The provisions of this recommendation do not apply to blood or blood derivatives.

4. For the purposes of this recommendation the term “organ and tissue trafficking” applies to:
   - the transportation of a person to a place for the removal of organs or tissues without his or her valid consent;
   - the transportation of a person to a place for the removal of organs or tissues with his or her consent but in contravention of legislation or other controls in operation in the relevant jurisdiction;
   - the transplantation of removed organs and tissues, whether transported or not, in contravention of legislation or other regulations in operation in the relevant jurisdiction or in contravention of international legal instruments.
5. For the purposes of this recommendation:
   - the term “transplantation” covers the complete process of removal of an organ or tissue from one person and implantation of that organ or tissue into another person, including all procedures for preparation, preservation, storage and transportation;
   - the term “removal” refers to removal from the body of an organ or tissue intended for transplantation, by a surgical procedure or by other means.

Article 3 – Prevention

Prevention of organ trafficking should be undertaken in an integrated way by:

   - improving organ and tissue availability by well-established means such as those described in the Council of Europe consensus document “Meeting the organ shortage: current status and strategies for improvement of organ donation” (1999);
   - approving a legal framework which strictly forbids any kind of commercialisation of the human body and its parts consistent with the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (ETS No. 164). Legislation should be extended to citizens going abroad. However, medical care should not be denied;
   - assuring the traceability of human organs and tissues through the accreditation and control of centres for procurement and/or transplantation, tissue banks, and the follow up of patients;
   - in the case of a living donor transplant, member states should provide for official authorisation of all such transplants;
   - in all cases where the living donor is a foreign citizen, the relevant officially recognised bodies in the country of transplantation and in the home country of the living donor must be informed;
   - in the case of a living donor, all payments to the donor should be strictly prohibited and considered a criminal offence.
This provision should not apply to payments which do not constitute a financial gain or a comparable advantage, in particular:

- compensation of living donors for loss of earnings and any other justifiable expenses caused by the removal or by related medical examinations;
- payment of a justifiable fee for legitimate medical or related technical services rendered in connection with transplantation;
- compensation in case of unjustified harm resulting from the removal of organs or tissues from living donors.

**Article 4 – Legal instruments**

1. Member states should ensure that there are legal instruments in place which prohibit the trafficking of persons for the purpose of organ or tissue transplantation and the trafficking of organs and tissues themselves.

2. Member states should ensure that those legal instruments prohibit:
   - the removal of organs and tissues except in centres or circumstances recognised for the purpose and by health professionals with appropriate training and experience;
   - the implantation of organs and tissues except in centres or circumstances recognised for the purpose and by health professionals with appropriate training and experience;
   - financial gain from the human body or parts of the body intended for transplantation;
   - advertising with the intention of securing persons or organs or tissues for trafficking or for financial gain;
   - organising or running an organisation or service involved in organ or tissue trafficking.

3. Member states shall ensure that legislation provides for appropriate sanctions to be applied in the event of any infringement of the provisions of this recommendation.
Recommendations of the Committee of Ministers to member states

Article 5 – The transplantation system

1. Member states shall ensure the provision of a nationally recognised transplantation system which guarantees equitable access to transplant services.

2. National transplant waiting lists should be established in compliance with the Committee of Ministers’ Recommendation Rec(2001)5 on the management of organ transplant waiting lists and waiting times.

3. The system shall ensure that:
   – appropriate information is recorded on all organs and tissues removed for the purposes of transplantation;
   – all organs, and where appropriate tissues, are only allocated to persons who are on a nationally recognised waiting list;
   – appropriate information is recorded on all organs and tissues used for implantation or other purposes;
   – information on the risks associated with organs obtained illegally is provided.

4. The information provided should ensure traceability from donor to recipient but shall be collected, processed and communicated in accordance with regulations relating to confidentiality and personal data protection.

Article 6 – International co-operation

1. Organ trafficking is a universal problem. Therefore international co-operation is required to combat it.

2. Member states should ensure full co-operation with all other states and with international agencies, including law enforcement agencies, in order to combat organ trafficking, and apply the sanctions provided for in this recommendation to any person or entity involved in organ trafficking.
3. Member states should present a full report of any allegations or instances of organ trafficking within their territory to the Secretary General of the Council of Europe.

Article 7 – Information for the general public

Member states should ensure that the general public is fully informed about organ trafficking and the penalties which may be incurred. In particular:

- accurate information about organ and tissue donation and transplantation should be provided;
- organ and tissue donation should be promoted as positive behaviour that contributes to saving lives and improving the health of many people;
- false reports on organ trafficking may alarm the general public and adversely affect organ and tissue donation and should be refuted.
Council of Europe
Committee of Ministers

Recommendation Rec(2004)8 of the Committee of Ministers to member states on autologous cord blood banks

(Adopted by the Committee of Ministers on 19 May 2004 at the 884th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common action in the field of health;

Taking into account Resolution (78) 29 on harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances and the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987);

Having regard to the European Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (ETS No. 164) and in particular to Articles 19 and 20 thereof;
Having regard to the Additional Protocol to the Convention on Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine concerning the Transplantation of Organs and Tissues of Human Origin (ETS No. 186);

Considering that:

The principal current use of blood cells collected at the time of birth from the umbilical cord (cord blood) is the collection of haematopoietic progenitor cells (HPC) that can be transplanted into patients with acquired or congenital diseases of the bone marrow. It is likely that such cells will, in the future, constitute a valuable source of cell therapies for the treatment of a wide range of diseases;

Cord blood stored only for autologous use, that is, by the donor or his or her immediate family, is only very rarely used. Furthermore, there is no scientific evidence that umbilical cord blood can be stored for long enough to be of any use to the vast majority of donors. Such storage could limit altruistic donation and thereby limit the possibility of treating those in need;

The unregulated collection of blood at the time of birth could distract the staff caring for mother and child at a critical time;

Even if it is the case that these children do, in the future, develop diseases requiring an HPC transplant, there is evidence to suggest that it is preferable to use allogeneic transplantation to achieve the “graft vs. tumour effect” in hematological diseases. In cases of congenital disease and in some leukaemias with intrauterine cell mutations, autologous HPC transplantation is contraindicated;

The health services of member states should only provide their citizens with proven clinical and cost effective therapies as resources are always limited;

With the aim of ensuring the availability of transplant treatments for an increasing number of people,
Recommendations of the Committee of Ministers to member states

Recommends to the member states that:

1. If cord blood banks are established, they should be based on altruistic and voluntary cord blood donation and used for allogeneic transplantation and related research;
2. The promotion of donation for autologous use and the establishment of cord blood banks for autologous use should not be supported by member states or their health services;
3. Accurate information should be provided to the population about the advantages and disadvantages of cord blood banks;
4. Where autologous cord blood banks are being established, the promotional material or information provided to families must be accurate, and fully informed consent to cord blood storage must be obtained;
5. Autologous cord blood banks that are being established must meet the quality and safety standards set out in the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells.
The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued *inter alia* by the adoption of common action in the health field;

Taking into account Resolution No. R (78) 29 on harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987); Articles 19 and 20 of the Convention of Human Rights and Biomedicine, and Articles 3 and 4 of the Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin;
Considering that:

- organ transplantation is a well-established, life-saving, and effective treatment: a successful organ transplantation may be the only treatment available for some forms of end stage organ failure and is the most clinically and cost effective treatment for chronic renal failure;
- organ exchange and circulation of recipients among member states is becoming a more frequent phenomenon, and that a minimum common standard should be guaranteed to the citizens;
- member states should therefore provide high-quality transplant services for the benefit of their citizens. Considering the limited organ supply, all necessary steps should be taken to make sure all available organs are properly safeguarded and used so as to maximise the benefit to patients;
- the highest professional standards are to be maintained in the area of organ transplantation,

Recommends that the governments of member states take all necessary measures to ensure the following:

1. An appropriate mechanism for the authorisation\(^1\) of health care facilities carrying out organ transplantations\(^2\) should be set up. In order to obtain authorisation these facilities should meet the following criteria:
   - feasibility of programme, based on clinical need assessment and a documented estimate of organ supply, to ensure that projected activity levels are sufficient to maintain clinical expertise and programme quality;
   - standards of vocational training of team members, and infrastructural conditions relating to availability of beds,

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\(^1\) For the purpose of this Recommendation, the term “authorisation” refers to any appropriate mechanism for designating, authorising, accrediting or licensing health care facilities carrying out organ transplantations.

\(^2\) This Recommendation refers to the facilities where organs are being “implanted”.

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intensive care facilities, and diagnostic and therapeutic back-up services (radiology, microbiology, immunology services, etc.), and to care provided by nursing, physiotherapy, social services and related medical professionals.

2. Medical professionals forming part of an organ transplant team should be properly qualified and their previous training in the field of transplantation should be documented and personalised.

3. A quality-management system should be put in place to evaluate performance against established national and/or international standards as applicable, and to ensure the quality of the process of organ procurement and transplantation, following the principles described in the Council of Europe's Guide to safety and quality assurance for organs, tissues and cells.

4. Authorisations should be regularly reviewed against agreed quality criteria and standards, as well as against audit results.

5. Outcome results for each type of transplant should be within the margins of international registers, at an equivalent degree of complexity of patients. In order to guarantee clinical results and cost-effective performance, minimal yearly activity standards shall be established in order to maintain an active programme.

6. These minimal activity standards, required to keep active each kind of transplant programme, should be related to the mean number of cadaveric organs available to the transplant team in recent years.

7. Any transplant centre which, after several warnings, continues to fail to meet activity or outcome criteria may have its authorisation withdrawn.

8. No new transplant centre may be authorised if there are not enough organs available to enable a new centre to reach the required standards.

9. Any new transplant centre should be authorised, accredited or licensed on the basis of agreed criteria and initially should be limited in time. If, within an agreed timescale, the new centre does not achieve the required standards, authorisation shall be withdrawn.
The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common action in the health field;

Taking into account Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances, the final text of the 3rd Conference of European Health Ministers (Paris, 16 and 17 November 1987); Articles 19 and 20
Recommendations of the Committee of Ministers to member states

of the Convention on Human Rights and Biomedicine, and Articles 3 and 4 of the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin, and principles established in the 1998 Council of Europe consensus document entitled “Meeting the organ shortage”;

Considering that organ transplantation is a well-established, life-saving, and effective treatment: a successful organ transplant may be the only treatment available for some forms of end stage organ failure and is the most clinically effective and cost-effective treatment for chronic renal failure;

Considering the universal shortage of organs for transplantation;

Considering that the transplant process is complex, involves various services and therefore requires effective organisation and co-ordination of health care professionals;

Bearing in mind that in many member states the training and employment of health care professionals responsible for detecting potential deceased organ donors and organising the donation process has increased the efficiency of the procurement of organs and improved the functioning of local and national transplant systems; and that such professionals can also increase the rate of donation of tissues for transplantation,

Recommends that the governments of member states take the measures contained in the appendix to this recommendation as regards the role and training of professionals responsible for organ donation (transplant “donor co-ordinators”).
Appendix to Recommendation Rec(2005)11

1. A professional responsible for the identification of potential deceased organ and/or tissue donors should be appointed in every hospital with an intensive care unit. This professional should have appropriate training and experience, be independent of any transplant teams, and have clearly defined responsibilities for the establishment, management and audit of a hospital-based system for potential deceased donor identification and organ/tissue procurement. The person should also be responsible for monitoring the donation and procurement process and for identifying and implementing improvements. For the purposes of this recommendation, the professional will be termed a transplant “donor coordinator”.

2. Donor co-ordinators should be properly accountable to senior management of the relevant health institution and to any regional or national transplant organisations. Donor co-ordinators may be complemented by, or responsible to, other transplant co-ordinators at regional or national level.

3. Donor co-ordinators, and any other transplant co-ordinators should have a high standard of professional training consistent with internationally recognised standards, to ensure the highest possible professional and ethical standards in organ donation and procurement. Member states should establish formal national or international accreditation for donor co-ordination activities/donor co-ordinators.
Council of Europe
Committee of Ministers

Recommendation Rec(2006)15 of the Committee of Ministers to member states on the background, functions and responsibilities of a National Transplant Organisation (NTO)

(Adopted by the Committee of Ministers on 8 November 2006 at the 979th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, in particular by the adoption of common rules in the public health field;

Bearing in mind the Convention on Human Rights and Biomedicine (ETS No. 164), in particular its Articles 19 and 20, and Article 3 of the Additional Protocol to the Convention on Human Rights and Biomedicine on Transplantation of Organs and Tissues of Human Origin (ETS No. 186);
Recalling its Recommendations to member states, Rec(2001)5 on the management of organ transplant waiting lists and waiting times, and Rec(2004)7 on organ trafficking, and recalling its Resolution (78) 29 on harmonisation of legislations of member states relating to removal, grafting and transplantation of human substances;

Considering that:

– organ transplantation is a well-established, life saving, and effective treatment. It may be the only treatment available for some forms of end stage organ failure and is the most clinically effective and cost effective treatment for chronic renal failure; tissue and cell transplantation may be life saving or life enhancing;
– organ transplantation, and sometimes tissue transplantation, is severely limited by the availability of organs for transplantation;
– a properly established and managed transplantation system is essential to maximise the rate of organ and tissue donation and provide equitable access to transplantation services for patients by guaranteeing the allocation of organs and tissues following rules which are transparent, objective and justified according to medical criteria, and by guaranteeing traceability and accountability,

Recommends that the governments of member states:

i. set up a comprehensive national transplantation system (NTS) for the authorisation¹, organisation and monitoring of organ, tissue, and cell donation and transplantation, taking into account the differences in the procedures of organ, tissue and cell donation and transplantation in member states;

ii. ensure that the NTS has a statutory basis which clearly sets out the structure of the system, its powers and responsibilities. It is preferable to have a single public body (a national transplant organisation (NTO)) which is officially recognised, and non-profit making with overall responsibility for donation, allocation,

¹ The term “authorisation” is meant to include the following three functions: accreditation, licensing, and designation.
traceability and accountability. However, a combination of local, regional, national and/or international bodies may work together to co-ordinate donation, allocation and/or transplantation, provided that the framework in place ensures accountability, cooperation and efficiency;

iii. ensure that the NTS has competencies and mechanisms to organise and oversee the whole process of transplantation including: public education on transplantation; organ (and tissue) donation and retrieval; national transplant recipient waiting lists; organ (and tissue) allocation; organ (and tissue) transportation including international exchanges; authorisation of organ transplant teams or institutions; the traceability of organs and tissues and monitoring of outcomes of transplantation and donations from living donors. Other NTS competencies may include research into transplantation and responsibility for identifying and reporting to the relevant authorities any breaches of the national transplantation law;

iv. implement the above recommendations taking into account the appendix to this recommendation.

Appendix to Recommendation Rec(2006)15

Transplantation is a complex process requiring a large number of functions to be managed effectively. Ideally, these functions should all be the responsibility of a single national transplant organisation (NTO), particularly with regard to organ transplantation. However, if the national transplantation system (NTS) integrates more than one structure, it is critical to ensure that the functions performed by each structure are appropriate, and complement those of the other transplant structures. The following allocation of functions is consistent with internationally recognised practice.
1. The essential functions of an NTO (with its advisory committees) are the following:

- running a central office which is operational 24 hours a day, 7 days a week, with which all donors have to be registered and which manages national or international organ allocation;

- ensuring that all relevant donor data, including screening results, are collected and communicated to the recipient’s transplant team;

- managing specific national waiting lists for organs, and, if applicable, for tissues, on the basis of agreed and transparent national admission criteria, containing sufficient up-to-date data on the recipient to ensure optimal matching;

- ensuring that all donated organs are allocated to the most appropriate recipient in compliance with nationally agreed and transparent allocation rules, to ensure as far as possible equal access to transplantation for all patients who could benefit from a transplant;

- ensuring that arrangements are in place for the safe and rapid transport of organs from the donor’s hospital to the recipient’s hospital;

- ensuring the maintenance of a transplant database of all donors and recipients, including follow-up data on living donors and recipients, to ensure traceability and to audit the outcome of transplant programmes;

- taking responsibility for running a transplant quality assurance system consistent with internationally recognised standards;

- providing accurate information to professionals on organ and tissue donation and the outcomes of transplantation as well as being responsible for professional education about transplantation and raising the awareness of the public about organ and tissue donation and transplantation;
Recommendations of the Committee of Ministers to member states

- ensuring complete transparency of national transplant procedures and processes in order to maintain or improve public and patient trust in the NTS;
- taking up national/international responsibility for tissue donation and transplantation.

2. The following functions should ideally be the responsibility of the NTO, or its advisory committees; alternatively they could be taken by other bodies in co-operation with the NTO:

- taking responsibility for the recruitment, training and appointment of donor transplant co-ordinators in all major hospitals likely to provide organ donors;
- taking responsibility for the co-ordination and management of donors and/or other transplant co-ordinators;
- conducting a regional/national potential donor audit to assess the total potential donor “pool” and identify reasons for non-donation;
- managing national organ donor/non-donor registers;
- reviewing donor screening methods and requirements to ensure compatibility with international standards and adapting them to any specific local requirements, if applicable;
- determining specific information requirements for organ and tissue donors;
- setting standards for donor management;
- setting standards for organ retrieval procedures, in particular multi-organ retrieval operations, in order to maximise organ quality and preservation;
- organising and co-ordinating organ donation and retrieval procedures;
- setting standards for organ and tissue packaging, labelling and transportation;
– organising the transport of organs and tissues from the donor's hospital to the recipient's hospital or tissue bank;

– setting criteria for the admission of patients to national organ or tissue-specific waiting lists;

– reviewing and analysing national transplant waiting lists, that is, waiting times according to demography, geography, etc., as a basis for recommending changes to allocations rules in order to ensure optimum allocation of organs;

– managing and analysing transplant data through the donation process, including an analysis of allocation, to ensure that the rules are properly applied and to prevent organ trafficking;

– taking responsibility for offering organs to other NTOs if a compatible recipient is not available;

– maintaining registers of all donors, including living donors, and all transplant recipients and/or designing and operating an integrated national transplant information system;

– in cases where a disease is transmitted to a recipient, identifying all other recipients of organs or tissues from that same donor, and/or allowing the retrieval and disposal of any unused organs or tissues;

– offering advice on the types of transplant that should be paid for by national health systems and any that may be allowed in the private sector;

– accrediting transplant teams and/or institutions allowed to perform organ and tissue transplants;

– inspecting and accrediting tissue banks in line with international standards, such as the standards set by the Council of Europe Guide to safety and quality assurance in organs, tissues and cells and the requirements set by the European Union Directive 2004/23/EC on setting standards for quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells;
Recommendations of the Committee of Ministers to member states

- managing and overseeing haemopoietic progenitor cell (HPC) transplants, including the importing of HPC cells;
- collecting data on outcomes and follow-up from transplant teams and units;
- auditing transplant procedures and outcomes to allow constant improvements in the safety and quality of organ transplantation;
- submitting outcome data to international transplant registers;
- organising and managing public relations and communication strategies on national transplantation issues;
- identifying patients registered on more than one national waiting list, and exposing possible cases of organ trafficking;
- setting standards for the screening and preparation of potential living donors;
- authorising living donor transplants, if foreseen by the NTS.

3. In view of a potential conflict of interest, the following function should not be the responsibility of the NTO but of a separate body, not related to a transplant organisation:

- setting the criteria to determine death either according to brain and brain stem failure or after cardiorespiratory failure to allow heartbeating and non-heartbeating organ donation, if foreseen by national law.

4. Member states wishing to collaborate within the framework of a supranational organisation should consider that the NTO should remain responsible for deciding on the functions to be allocated to an international body.
Council of Europe
Committee of Ministers

Recommendation Rec(2006)16 of the Committee of Ministers to member states on quality improvement programmes for organ donation
(Adopted by the Committee of Ministers on 8 November 2006 at the 979th meeting of the Ministers’ Deputies)

The Committee of Ministers, under the terms of Article 15.b of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued in particular by the adoption of common rules in the public health field;

Taking into account Resolution (78) 29 on harmonisation of legislations of member states relating to removal, grafting and transplantation of human substances, the final text of the 3rd Conference of European Health Ministers (Paris, 16 and 17 November 1987), Articles 19 and 20 of the Convention of Human Rights and Biomedicine (ETS No. 164), and Articles 3 and 4 of the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin (ETS No. 186);
Considering that:
- organ transplantation is a well-established, life saving, and effective treatment. It may be the only treatment available for some forms of end stage organ failure and is the most clinically effective and cost effective treatment for chronic renal failure;
- member states should provide high quality transplant services for the benefit of their citizens. Considering the organ shortage, all necessary steps should be taken to ensure that all available organs are properly safeguarded and used so as to maximise the benefit of patients;
- the process of organ donation and transplantation is a complex process which involves a long series of stages which should be followed rigorously in order to be effective. Each of these stages should be analysed whenever a problem arises in order to detect weaknesses in the process and take the necessary corrective measures;
- the document “Meeting the organ shortage” approved by the Council of Europe, states the need to develop a protocol to identify potential donors, including the registration of donors, and to clarify the roles and responsibilities of hospital professionals in donor identification,

Recommends that the governments of member states take all necessary measures to ensure that:

i. a quality improvement programme for organ donation is put in place in every hospital where there is a potential for organ donation;

ii. the quality improvement programme is primarily a self-evaluation of the whole process of organ donation, jointly performed by the specialists in intensive care and the transplant co-ordinator of every hospital. Whatever the nature of the programme, it should represent an appropriate mechanism for monitoring the whole process of organ donation in intensive care units;

iii. the hospital programme is harmonised at regional and national level in order to compare adequately the results obtained and to adopt the most appropriate measures to improve organ donation;
iv. external audits performed by experts from other hospitals, regions or countries are performed regularly after the implementation of the self evaluation programme, in order to further improve the process and provide greater transparency;

v. the objectives of these programmes include:
   – definition of the theoretical capacity of organ procurement, depending on the characteristics of the hospital;
   – detection of obstacles to the process of organ donation and procurement and analysis of the causes of potential donor losses, as a tool to identify areas for improvement;
   – a description of factors with regard to hospitals which can influence the donation and transplantation process;

vi. a systematic review of all medical records of patients who have died in intensive care units (ICU) and possibly in other similar units is performed on a regular basis in order to analyse any undetected potential donor and establish means for improvement;

vii. in every hospital, region and country the following data must be periodically monitored:

   **General data:**
   – number of available hospital beds;
   – number of available ICU beds;
   – number of neurosurgery procedures;
   – number of patients admitted to the ICU and emergency rooms;

   **Specific data:**
   – hospital deaths;
   – brain deaths;
   – number of potential organ donors;
   – number of organ donors;

viii. appropriate standards must be defined in every country according to the characteristics of the hospital and the health system in order to compare the results with those of other regions or countries, so as to better define the areas for improvement.
Resolutions
The Committee of Ministers,

Considering that the aim of the Council of Europe is to achieve a greater unity between its members, in particular through harmonising legislations on matters of common interest;

Considering that because of the substantial increase in recent years in the treatment of patients by transplantation or grafting of removed human organs, tissues, or other substances, the need for new and more specific legislation was felt in all member states;
Considering that harmonisation of legislations of member states on removal, grafting and transplantation of human substances will ensure better protection of donors, prospective donors and recipients of human substances and enhance the progress of medical science and therapeutics;

Recommends to the governments of member states:

a. to conform their laws to the rules annexed to this resolution or adopt provisions conforming to these rules when introducing new legislation;

b. to introduce appropriate sanctions to ensure the application of the rules adopted when implementing this resolution;

c. to study the desirability and the possibility of inserting in an appropriate document a statement so that the wish of the deceased person as mentioned in Article 10 of the rules might be determined more easily;

d. to intensify, by appropriate means, their efforts to inform the public and arouse the interest of doctors in the need and importance of donations of substances, while keeping the confidential character of individual operations;

e. to provide, or to encourage the preparation of practical guidelines for those entitled to decide according to paragraph 1 of Article 11 that a substance may be removed from a deceased person;

f. to apply the rules annexed to this resolution, in particular Articles 9 and 14, to substances originating from states which are not members of the Council of Europe.

Invites the governments of member states to inform the Secretary General of the Council of Europe in due course and at any rate every five years, of the action taken on the recommendations contained in this resolution.
RULES

Chapter I – Field of application

Article 1
1. These rules apply to removals, graftings, transplantations and other use of substances of human origin removed or collected for therapeutic or diagnostic purposes for the benefit of persons other than the donor and for research purposes.
2. The transfer of embryos, the removal and transplantation of testicles and ovaries and utilisation of ova and sperm are excluded from the field of application of these rules.

Chapter II – Removals, graftings and transplantations of substances from living persons

Article 2
1. The donor and his legal representative in the case of a minor or otherwise legally incapacitated person (both hereafter referred to as “legally incapacitated person”), must be given appropriate information before the removal about the possible consequences of this removal, in particular medical, social and psychological, as well as the importance of the donation for the recipient.
2. The anonymity of the donor and of the recipient must be respected except where there are close personal or family relations between the two.

Article 3
A removal must not be effected without the consent of the donor. This consent must be given freely.
In cases of removal of substances which can regenerate which presents risks for the donor and of removal of substances which cannot regenerate, this consent must be given in writing.

Article 4
Removal of substances which cannot regenerate must be confined to transplantation between genetically related persons except in exceptional cases where there are good chances of success.

Article 5
Where removal of substances presents a foreseeable substantial risk to the life or the health of the donor, a removal may only be permitted exceptionally when it is justified by the motivations of the donor, the family relationship with the recipient and the medical requirements of the case. However a state can prohibit such removal.

Article 6
1. For legally incapacitated persons removals of substances which can regenerate must be limited to exceptional cases. Such a removal may be permitted when it is necessary for therapeutic or diagnostic reasons. It may only be effected with the consent of the legal representative of the incapacitated person if the incapacitated person does not, himself, object to it. If the removal represents a risk to the health of the incapacitated person, prior authorisation must also be obtained from an appropriate authority.

2. The removal of substances which cannot regenerate, from legally incapacitated persons is forbidden. However, a state may permit such a removal in a special case justified for therapeutic or diagnostic reasons if the donor, having the capacity of understanding, has given his consent, if his legal representative and an appropriate authority have authorised removal and if the donor and the recipient are closely genetically related.

3. A removal of substances which presents foreseeable substantial risk to the life or the health of the donor who is a legally incapacitated person is forbidden.
Article 7
Before the removal and transplantation appropriate medical examinations must be made to evaluate and reduce the risks to the health and life of both donor and recipient.

Article 8
1. Substances must be removed under conditions representing the least possible risk to the donor.
2. Removals, graftings and transplantations of substances which cannot regenerate must take place in properly equipped and staffed institutions.

Article 9
No substance may be offered for profit. However, loss of earnings and any expenses caused by the removal or preceding examination may be refunded. The donor, or potential donor, must be compensated, independently of any possible medical responsibility, for any damage sustained as a result of a removal procedure or preceding examination, under a social security or other insurance scheme.

Chapter III – Removals, graftings and transplantations of substances from deceased persons

Article 10
1. No removal must take place when there is an open or presumed objection on the part of the deceased, in particular, taking into account his religious and philosophical convictions.
2. In the absence of the explicit or implicit wish of the deceased the removal may be effected. However, a state may decide that the removal must not be effected if, after such reasonable inquiry as may be practicable has been made into the views of the family of the deceased and in the case of a surviving legally incapacitated
person those of his legal representative, an objection is apparent; when the deceased was a legally incapacitated person the consent of his legal representative may also be required.

Article 11
1. Death having occurred a removal may be effected even if the function of some organ other than the brain may be artificially preserved.
2. A removal can be effected if it does not interfere with a forensic examination or autopsy as required by law. A state may, when such requirement exists, decide that a removal can only be effected with the approval of a competent authority.

Article 12
1. Removals for therapeutic, diagnostic or research purposes must be effected in appropriate places and under suitable conditions.
2. Grafting and transplantations must take place in public or private institutions which possess proper staff and equipment.
3. Death must be established by a doctor who does not belong to the team which will effect the removal, grafting or transplantation. However, this doctor can effect a removal in cases of minor operations when no other suitable doctor is available.

Article 13
The identity of the donor must not be disclosed to the recipient and the identity of the recipient to the family of the donor.

Article 14
Substances must not be offered for any profit.

(Adopted by the Committee of Ministers on 12 March 2008 at the 1021st meeting of the Ministers' Deputies)

The Committee of Ministers, in its composition restricted to the representatives of the States Parties to the Convention on the elaboration of a European Pharmacopoeia,1

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common action in the public health field;

Having regard to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and

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1 States concerned: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "the former Yugoslav Republic of Macedonia", Turkey and United Kingdom.
Biomedicine – ETS No. 164), and in particular Article 19 (General rule) and Article 20 (Protection of persons not able to consent to organ removal) thereof;

Having regard also to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin (ETS No. 186), and, in particular, Chapter III (Organ and tissue removal from living persons);

Recalling its Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances;

Recalling its Recommendation Rec(2001)5 to member states on the management of organ transplant waiting lists and waiting times;

Recalling its Recommendation Rec(2004)7 to member states on organ trafficking;

Recognising that, in facilitating the transplantation of organs in the interest of patients in Europe, there is a need to protect individual rights and freedoms and to prevent the commercialisation of parts of the human body involved in organ procurement, exchange and allocation activities;

Considering that organ transplantation is a well-established, life-saving, and effective treatment and may be the only treatment available for some forms of end-stage organ failure;

Aware of the fact that tissue and cell transplantation may be life saving or life enhancing;

Concerned by the universal shortage of organs for transplantation;

Considering that adult-to-adult living donor liver transplantation (Domino liver transplantation, i.e. transplantation into a recipient whose own organ was respected and transplanted into another recipient, is excluded from the scope of this resolution) may be envisaged when suitable organs from deceased donors are not
available, provided that all safeguards are implemented in order to guarantee the freedom and safety of the donor and a successful transplant in the recipient;

Convinced also that adult-to-adult living donor liver transplantation is an effective treatment for end-stage liver disease, with the potential benefit of reducing mortality of patients awaiting a transplantation;

Conscious of the risks that living donor liver transplantation may have for the donor and of the need to ensure that all measures are taken to safeguard the donor’s health;

Recalling that no organ removal may be carried out on a person who does not have the capacity to consent;

Recommends to member states the following:

1. to instruct the organisation responsible for accrediting transplantation programmes and regulating the allocation of organs to address explicitly the issue of adult-to-adult living donor liver transplantation and establish transplantation programmes accredited to perform this type of transplantation;

2. to ensure that adult-to-adult living donor liver transplantation programmes adhere to the following minimum requirements:
   a. substantial experience in liver surgery and liver transplantation;
   b. an active liver-transplantation programme;
   c. significant mortality in the waiting list;
   d. a multidisciplinary team experienced in routine and complex liver surgery, covering all operative aspects (pre-operative, peri-operative and post-operative);

3. to ensure that the indications for adult-to-adult living donor liver transplantation are recognised indications for deceased donor liver transplantation;

4. to ensure that the organisation responsible for the allocation of organs and accreditation of transplantation programmes establishes
clear conditions under which adult-to-adult living donor liver transplantation is ethically acceptable, namely:

a. adult-to-adult living donor liver transplantation is only to be performed within authorised/licensed programmes with ongoing feedback;

b. the donor and the recipient have a close personal relationship as required and defined by law;

c. each single procedure should be approved on a case-by-case basis;

d. the motive to donate is solely altruistic. Any financial gain or comparable advantage in connection with the donation is considered illegal;

e. the donor has been given appropriate information as to the purpose and nature of the removal as well as on its consequences and risks. The donor has also been informed of the rights and the safeguards prescribed by law for his or her protection, in particular of the right to have access to independent advice about such risks by a health professional having appropriate experience and who is not involved in the organ removal or subsequent transplantation procedures. Finally, the donor is provided with comprehensive information on:

   i. the alternatives to adult-to-adult living donor liver transplantation;

   ii. the previous experience of the centre where the procedure will be carried out;

   iii. the risks of morbidity and mortality of the procedure for the donor and the recipient;

   iv. the likely long-term outcome for the recipient;

f. the living donor has given free, informed and specific consent either in written form or before an official body; the donor may freely withdraw consent at any time;
g. the donor has been properly screened to identify any physical or psychological contra-indication; the removal may not be carried out if there is a serious risk to the life or health of the donor;

5. to ensure immediate access to the emergency waiting list for organs from deceased donors in case of failure of the remnant liver in the donor or graft failure in the recipient and that specific rules for non-residents apply according to national regulations;

6. to ensure that the necessary conditions and provisions are in place for long-term medical follow up of both donor and recipient, including the monitoring of the short- and long-term effects of transplantation on the health of donors, by the establishment of national registries;

7. to guarantee equitable access to liver transplantation services for all patients in need of a liver transplant, regardless of personal financial means;

8. to ensure that all costs related to the operations and follow-up of donor and recipient are covered, according to the competent organisation’s own procedures;

9. to provide for a system of fair compensation for any person who suffered undue damage resulting from transplantation procedures, according to the conditions and procedures prescribed by law.
Resolution CM/Res(2008)6 on transplantation of kidneys from living donors who are not genetically related to the recipient

(Adopted by the Committee of Ministers on 26 March 2008 at the 1022nd meeting of the Ministers’ Deputies)

The Committee of Ministers, in its composition restricted to the representatives of the States Parties to the Convention on the Elaboration of a European Pharmacopoeia,¹

Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common action in the health field;

¹ States concerned: Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, Republic of Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, “the former Yugoslav Republic of Macedonia”, Turkey and United Kingdom.
Taking into account its Resolution (78) 29 on the harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances and the final text of the 3rd Conference of European Health Ministers (Paris, 16-17 November 1987);

Having regard to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine – ETS No. 164), and in particular to Article 19 (General rule) and Article 20 (Protection of persons not able to consent to organ removal) thereof;

Having regard also to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning the Transplantation of Organs and Tissues of Human Origin (ETS No. 186);

Recalling its Recommendation Rec(2001)5 to the member states on management of organ transplant waiting lists and waiting times;

Recalling its Recommendation Rec(2004)7 to the member states on organ trafficking;

Recognising that, in facilitating the transplantation of organs in the interests of patients in Europe, there is a need to protect individual rights and freedoms and to prevent the commercialisation of parts of the human body involved in organ procurement, exchange and allocation activities;

Recalling the principle that organ removal can be undertaken on a living donor only in the case where a suitable organ from a deceased donor is not available and only when no alternative therapeutic method of comparable effectiveness is available;

Considering that there is a shortage of kidneys for transplantation to patients having reached the end stage of renal failure;

Taking note that the increasing number of transplantations of organs from living donors is one way of reducing the increasing gap between the growing number of patients waiting for kidney transplantation and the limited number of organs procured from deceased donors;
Stressing that transplantation of a kidney from a living donor to a genetically related recipient is a well-established practice in most of the States Parties to the Convention and that in some countries living donor kidney transplantations account for a large proportion of the transplants performed each year;

Knowing that there is very good evidence that living donor kidney transplants, even if the donor is not genetically related to the recipient, lead to similar or better clinical outcomes than with kidneys transplanted from deceased donors;

Stressing that living donor kidney transplants allow for the optimum treatment of receiving a transplant before going on to dialysis (pre-emptive transplant);

Taking into consideration that the removal of a kidney from a carefully selected, healthy individual carries a low risk of complications and has not been shown to have long-term effects on the health of such a donor;

Recalling that no organ removal may be carried out on a person who does not have the capacity to consent,

Recommends to the governments of States Parties to the Convention to take note of the general principles and measures listed in the attached appendix when they draw up the regulations and procedures relating to the donation of a kidney in view of transplantation by a living donor non genetically linked to the receiver.

Appendix to Resolution CM/Res(2008)6

1. States Parties to the Convention may permit the transplantation of kidneys from non-genetically related living donors on condition that:
   – the living donor and the recipient have a relationship as required and defined by law; the donor has been given appropriate
information as to the purpose and nature of the removal as well as on its consequences and risks. The donor has also been informed of the rights and the safeguards prescribed by law for his or her protection, in particular of the right to have access to independent advice about such risks by a health professional having appropriate experience and who is not involved in the organ removal or subsequent transplantation procedures;

- the living donor has given free, informed and specific consent, either in written form or before an official body; the donor may freely withdraw consent at any time;
- no pressure is exerted on the living donor into donation;
- the organ does not, as such, give rise to financial gain or comparable advantage;
- the living donor has been properly screened to identify any physical or psychological contraindications; the removal may not be carried out if there is a serious risk to the life or health of the donor;
- long-term medical follow-up is provided to living donors. This includes the monitoring of short-and long-term effects of organ removal on the health of the living donor notably by the establishment of officially recognised registries.

2. States Parties to the Convention may require that persons waiting for such transplants be placed on a national waiting list during the period of approval of the potential donor for donation.

3. Any States Parties to the Convention allowing for non-genetically related living kidney donation should establish a register for such transplants which includes a donor register and donor follow-up procedures in line with those existing for transplantations of kidneys removed from genetically related living donors.

4. States Parties to the Convention may permit or prohibit by law non-directed living kidney donations – i.e. “good Samaritan” donors, truly altruist donors or donors involved in a “paired exchange” donation for the purpose of transplantation from a person with no established close personal relationship with the recipient. (This
type of donation is in contrast to donation where the donor and the recipient are in close personal relation called “directed donation”).

In the States Parties to the Convention authorising donations from non-related living donors, national regulations and appropriate management must be put in place in view of prohibiting and preventing organ trafficking, namely by clearly defined rules for non-residents.

5. States Parties to the Convention should establish an independent mechanism for approving non-genetically related living kidney donor transplants in compliance with Article 10 of the Additional Protocol to the Convention on Human Rights and Biomedicine concerning the Transplantation of Organs and Tissues of Human Origin. It is also recommended that States Parties to the Convention establish such a mechanism for all cases of non-directed donation. Particular attention should be given to cases where the donor is not a resident of the member state concerned. Within the requirements of data protection legislation, registered activities should be reported on a regular basis to the national health authority.
Reports
Organ shortage: current status and strategies for improvement of organ donation – A European consensus document

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The following definitions will be used throughout this document:

**Transplantation** – The procedure, comprising a series of technical steps which need to be followed in a defined order, that enables the organs (or tissues) obtained from dead people (donors) to be transplanted into an appropriate live donor. It starts with the identification of all potential donors and ends with the transplantation (or storage) of the organs (and/or tissues) retrieved.

**Brain Death** – Complete and irreversible cessation of all cerebral and brain stem functions which, from the scientific, ethical and legal point of view is accepted as equivalent to the death of the individual. Strict testing according to agreed protocols is required to establish brain death beyond doubt.

**Potential Donor** – Any person diagnosed as brain dead, by means of clinical examination, following the elimination of any medical contraindications to donation, i.e. conditions representing a potential risk for recipients.

**Effective Donor** – A potential donor from whom at least one solid organ (or tissue) has been retrieved for transplantation.

(Potential and/or effective donor rates can be expressed either by reference to the catchment population (donors per million population – pmp) or by reference to hospital parameters (e.g. donors as a percentage of overall hospital mortality; of intensive care mortality or as a rate per hundred hospital beds, etc.)).
Retrieval – removal of an organ or tissue intended for transplantation whether subsequently transplanted or not.

Key Donation Person: A person responsible for organ donation in a specific area or hospital. He/She may or may not be the transplant co-ordinator.

Organ Sharing Office (OSO): Bureau responsible for the collection and management of data from donors and recipients and allocation of organs according to agreed criteria.

Organ Exchange Organisation (OEO): Organisation responsible for the organ +/- tissue allocation in a specific region/country.

Organ Procurement Organisation (OPO): A body or organisation responsible for organ donation and procurement in a specific region/country.

1 In some countries one organisation may perform more than one or all of the above functions within a region or country.
1. Summary

1.1. Organ transplantation is the best available established technique for the treatment of end stage failure of most essential organs (liver, heart and lungs). Corneal transplantation is similarly well established and tissue transplantation, particularly of bone but also of skin, tendons, etc., is growing very rapidly. Over 1 million people world-wide have benefited from successful organ transplantation. A number of transplant patients have survived well over 25 years and five years survival rates for most organ transplant programmes are around 70%. With modern techniques of organ preservation and advances in immuno-suppression, a significant proportion of patients can now expect to achieve long-term survival with a high quality of life.

1.2. Many more people could benefit from organ transplantation than receive transplants at present. There are currently nearly 40,000 patients waiting for a kidney in Western Europe. Mortality rates for patients waiting for a heart, liver or lung range between 15% and 30%, i.e. 400 plus die waiting for an organ each year. These figures do not represent the true position. Because of the chronic shortage of organs, some transplant clinicians are extremely selective about the patients they put on the waiting list. Currently only those patients most likely to benefit will be even considered for transplantation.

1.3. The critical factor is the supply of organs for transplantation. Only good quality organs are likely to function satisfactorily and there are strict limits on the time that can be taken to retrieve and
transplant the organ. In practice this means that, for most organs, only relatively young donors are suitable who are admitted into intensive care units and subsequently declared brain dead so that organs can be retrieved while the donors heart is still beating. A typical donor has suffered either a road traffic accident or a severe cerebrovascular accident. Due to improvements in road safety in European countries, donors in the former group are in decline. Kidneys are somewhat less sensitive to ischaemia (shortage of oxygen).

1.4. In view of the potential for successful transplantation, it is considered essential that countries with an organ transplant service, take all possible measures to ensure that all potential donors are identified and as many as possible converted into effective donors.

1.5. The organ donation/transplantation process is necessarily complex. There is a number of important steps each of which needs to be recognised and an effective system put in place to manage that every part of the process if potential donor organs are not to be lost. The steps are:

i. **Donor identification** – all potential donors should be identified at as early a stage as possible. This will facilitate donor screening and donor management (see below).

ii. **Donor screening** – donors should not be used if there is a risk of transmission of serious disease (cancer, infection) to the recipient. Guidance has been prepared by the Council of Europe and some member states on the serological and other screening methods that should be used to minimise the risk of transmission of infectious or malignant diseases to the recipient. Whenever possible, screening should include a social history taken from the relatives to exclude recent high risk behaviour, which might indicate a risk of a transmissible disease which is at too earlier stage to be detected by serological screening.
iii. **Donor management** – it is essential that organs procured are in good condition prior to retrieval. The management of the potential donors physiological state while on intensive care and of the donor prior to and during retrieval can make a major difference to the condition of the organs. Poor donor management can make organs unusable.

iv. **Consent/authorisation** – appropriate consent or authorisation has to be obtained before organs can be removed. Countries have different legal requirements, in some consent is presumed while in others specific consent has to be sought from either relatives or some body. Whatever the system, it is advisable to discuss donation with any relatives as part of the screening process. There is evidence that the approach to the relatives can affect their willingness to agree to donation. Staff seeking to obtain the agreement of relatives should be appropriately trained.

v. **Organ retrieval** – the surgical technique for removing organs from the body and the way those organs are subsequently handled and preserved prior to and during transportation are critical to the successful outcome of the transplant. Each year a number of organs are damaged during removal and/or transportation. Some can be repaired but a few will have to be discarded.

vi. **Organ allocation** – for some organs, particularly kidneys, the successful long-term outcome of the transplant depends partly on appropriate matching between donor and recipient. A well-organised system for allocating and transporting donated organs to the most appropriate recipient is important. In some cases, optimum allocation will require exchange of organs or tissues between transplant organisations and countries. Co-operation between countries is increasingly important.

1.6. The purpose of this document is to provide a step-by-step guide to the most effective ways of procuring the maximum number
of high quality organs for transplantation from cadaveric donors based on an analysis of the scientific data available and relevant international experience. Recommendations are made on the most effective ways of procuring organs from such donors and for monitoring the procurement process. In making the recommendations, local and national requirements and the legal, ethical and cultural frameworks within which individual countries have to operate have been taken into account.

1.7. If at each stage of the process and level of organisation, certain key objectives can be met, countries can maximise the rate of organ transplantation.
2. Summary of recommendations

2.1. Organ procurement

i. The transplant process is long and complex and cannot be left to chance. Protocols should be developed for each step. A key person should be made responsible in each area/hospital for managing and monitoring the process with the power to determine where efforts and resources should be directed.

ii. Published figures cannot be extrapolated to provide local rates of potential versus effective donors (although marked differences from published rates for potential donors should be considered as suggestive of under detection). A donor detection gap should be established for each hospital/area and systems for monitoring the rates established.

iii. A means should be developed to evaluate the size and characteristics of the potential donor pool to measure and monitor potential donor detection rates. To ensure reliability, data should be collected prospectively and analysed retrospectively as recommended in the “Donor Action Programme”.

iv. Proactive donor detection programmes should be instituted in every acute hospital using specially trained professionals (key donation persons) working to agreed protocols and ethical rules.

v. A “key donation person”, independent from transplant teams, should be appointed in every acute hospital with a clearly defined role and responsibility for establishing, managing and auditing systems for donor identification and identifying potential areas for improvement.
vi. Protocols should be developed setting out the criteria for screening potential donors and their organs for the risk of disease transmission and potential viability. All appropriate steps should be taken to avoid the transmission of infectious and neoplastic diseases and primary organ failure.

vii. The incidence of irreversible cardiac arrest, sepsis and other contraindications to organ donation relating to donor management of potential donors should be monitored and audited to detect and correct any problems identified. Involvement of Intensive Care Unit staff in research and/or educational programmes on donor management should help raise standards.

viii. An appropriate legal framework for donation and transplantation is required which adequately defines brain death; the type of consent or authorisation required for retrieval (see below); the means of organ retrieval, which ensures traceability but maintains confidentiality and which bans organ trafficking.

ix. Law professionals should be fully aware of the transplant process and the co-operation of those most closely involved, i.e. judges and coroners, should be sought to reduce legal refusals to a minimum.

x. It is advisable to ascertain the opinion of the public and health professionals about presumed or informed consent for organ donation before considering legal changes that might be potentially detrimental. The key donation person appointed in each centre/area must be aware of all local legal criteria and should be responsible for meeting these requirements. There should be a system for the safe custody of all certificates and test results required by the law.

xi. Because both positive and negative messages can affect the public's willingness to donate organs, there is a need for a professional attitude towards, and support from experts in the field of, communications. They should help to minimise the impact of “bad news” on, and to maximise the communication
of “good news” about transplantation to, health professionals, the media and the public. Special attention should be paid to both the content of the message and the best means of dealing with the most controversial topics. The preparation of specific briefing materials should be considered.

xii. The most cost effective means of increasing the publics willingness to donate seems to be improving the knowledge of health professionals (not directly involved in transplantation) and the media about transplantation issues. Continuing education should form an essential element of any communication strategy. A transplant hotline manned by appropriately trained professionals should be considered.

xiii. People should be encouraged to speak about organ donation and transplantation and to communicate their wishes to their relatives. As a donor’s wishes will not always be known, staff in a position to make requests for agreement to organ donation to relatives should be properly trained for the purpose. If such requests are well handled the rate of donation refusals can be reduced.

xiv. Organ retrieval procedures should be well planned to minimise delay and disruption to donor hospital. Retrieval teams should be lead by experienced surgeons trained, where appropriate, in multi-organ retrieval. Organ damage during retrieval should be reported and monitored and further training provided as necessary to minimise damage during retrieval or transportation.

xv. An organ sharing/allocation organisation is essential but its roles and responsibilities must be clearly defined, particularly if it is to have a role in organ donation and procurement (see below).

xvi. Attention should be paid to ensuring that hospitals are properly resourced and, if necessary, reimbursed for maximising organ procurement.

xvii. In order to optimise organ donation there is need for a supra hospital transplant organisation, appropriate in size and structure to the local situation with specific responsibilities for the whole process of organ procurement.
xviii. The most effective organisational approach is one which balances the requirements for effective organ procurement (small, local) with those for organ allocation (large, national/multinational) (see below). The aim should be to optimise organ procurement whilst ensuring the most clinically effective allocation of organs and tissues.

xix. Health Administrations are responsible for ensuring that there is proper organisational support for organ donation and distribution and should guarantee the fairness, transparency and safety of the whole system.

2.2. International co-operation

xx. International co-operation on the promotion of organ donation is desirable to help maximise organ donation and equalise access to transplantation between countries. Governments should actively promote such co-operation.

xxi. Priority should be given to international co-operation which improves standards of training, exchange of experience, and which helps guarantee the safety of organs and the ethical standards by which they are retrieved and transplanted.
3. Introduction

After four decades of experience, progress in transplantation medicine and surgery has been impressive. Advances in technique and the development of new immunosuppressive drugs have made it possible to transplant successfully several major organs, i.e. kidney, heart, heart/lung, lung and liver, into an increasingly large number of patients. Transplants of the pancreas and small bowel are also being performed. Over 1 million people world-wide have received an organ transplant and some have already survived more than 25 years. Five-year survival rates for most organs are now at least 70%. Transplantation of parts of organs or tissues including corneas, heart valves, bone, tendons, etc. are also well established and in some cases like bone, demand is growing very rapidly.

However, a severe shortage of cadaveric organ donors remains a major obstacle preventing the full development of transplant services and imposes a severe limit to the number of patients who benefit from this form of therapy. Although organ transplants save thousands of lives and transform the quality of life of thousands more, many people will die or remain on renal replacement therapy because the organ supply falls drastically short of demand. Nearly 40,000 patients are at the moment waiting for a kidney in Western Europe whilst the number of cadaveric donors remains stable at around 5,000 each year.\(^1\) This is also the case in USA where the gap between the number of available organs and patients on the waiting list is also very high. They have more than 30,000 patients on the waiting list and the number of cadaveric donors is around 5,000 each year.\(^2\) Mortality rates while
waiting for a heart, liver or lung transplant generally range between 15% and 30% but are even higher in some reports depending on the type of the organ needed. In 1994 there were no suitable livers for some 400 European citizens and around a further 400 died while waiting for a heart.

These figures do not reveal the true levels of unmet need for such organs. The potential need for the different organs is much higher. The shortage of organs means that only the patients most likely to benefit are put on the waiting list for an organ transplant. To put patients on a waiting list who have no hope of receiving an organ is both pointless and highly questionable ethically.

The increasing demand for organs with no increase in the supply poses problems for many countries, particularly countries in which regulation of live donation is nonexistent or poorly regulated, as the risk of organ trafficking increases. In some countries outside Europe, adults have voluntarily sold one of their kidneys in exchange for money or some other kind of compensation. There have been rumours of kidnapping and coercion to force the donation of a kidney although these are fortunately mostly unfounded. Organ trafficking not only poses major ethical problems, but also makes it more difficult to guarantee the quality and safety of the organ. Organ donation, properly regulated, allows the safety and quality of the organs to be properly assessed. For this reason there is now a strong international consensus that, until or unless some alternative such as xenotransplantation becomes available, the only acceptable course of action is to make every effort to maximise the procurement of cadaveric organs for transplantation. Member states of the Council of Europe and the European Union and their respective transplant organisations have taken steps to eliminate the possibility of coercion or organ trafficking. Specifically, Article 21 of the Convention on Human Rights and Biomedicine states “the human body and its parts shall not, as such, give rise to financial gain”.

Transplantation comprises the processes of organ donation and subsequent implantation or grafting. The two parts are totally
interdependent. However, historically, the techniques of organ implantation have received far more attention from the scientific community in terms of both research effort and resources than organ and tissue procurement. Until very recently, only 2-3% of papers submitted to International transplant meetings were devoted to organ donation, procurement and preservation. Most transplant professionals now recognise the severity of the organ shortage and the need to address the problems posed. Editorials in specialist journals have recently addressed the problem,\(^{5,6}\) but there are still few research papers in this field.

Increasingly, national health departments, international working groups and meetings of experts are seeking to develop a closer co-operation between health professionals and administrations. Private companies and foundations are also now dedicating financial resources to support the development of educational or research programmes relating to organ procurement. The programmes of all international transplant meetings now include sessions devoted to organ procurement. However, organ procurement is not just a matter for transplant teams. The whole medical community needs to be aware of the problem and become involved either indirectly or directly in the process of organ procurement. Indirectly health care professionals can educate others about the problem, allay fears and encourage a positive attitude to donation. Directly, all health care staff can help identify potential donors and ensure that such patients are recognised and assessed. As in any other medical activity, the overall success of transplantation is ultimately the responsibility of all health care professionals.

This document provides an analysis of the steps necessary to achieve an effective process for organ procurement taking into account the available scientific evidence and describing relevant international experience. The document focuses on the technical and organisational aspects of cadaveric organ donation.

It should however be remembered that the deceased’s wishes and the sentiments of his/her family have to be treated with respect.
The communication established with the deceased's family and the consideration given to their wishes are essential elements in the process of procurement itself.

Recommendations are made wherever opportunities exist for improving the process.

This document does not discuss living donation.

It does not discuss organ retrieval from non-heart beating donors (NHBDs) either, since such techniques are not currently universally accepted due to additional ethical, legal, technical and organisational problems.
4. Organ procurement

4.1. The transplantation process

4.1.1. Overview

Transplantation is a complex process involving a number of discrete but interconnected steps. Before considering the practicalities of the process, it is important to recognise the context within which it takes place. The use of substances derived from one human being for the treatment of others imposes unique ethical questions for society, particularly when, in the case of organs and most tissues, those substances are not renewable. Society now demands this type of treatment and itself benefits from the results. As Arthur Caplan testified before the US congress in 1990:

“What is truly distinctive about transplantation is not technology or cost, but ethics. Transplantation is the only area in all of health care, which cannot exist without the participation of the public. It is the individual citizen who while alive, or in the case of vital organs, after death, who makes organs and tissues available for transplantation. If there were no gift of organs or tissues, transplantation would come to a grinding halt.”

Essentially, any acceptable organ transplant service depends totally on altruistic organ donation by either living or cadaveric donors. However, the Convention on Human Rights and Biomedicine states that:

“Removal of organs or tissue from a living person for transplantation purposes may be carried out solely for the therapeutic benefit of the
recipient and when there is no suitable organ or tissue available from a deceased person and no other alternative therapeutic methods of comparable effectiveness.”

When considering aspects of the transplant process, these important societal principles have to be taken into account.

Health professionals are essential to transplantation, as transplants are medical procedures. Such factors as economic benefit, institutional or individuals reputations, surgical ego, municipal pride or chauvinism, however, should never be the *raison d’être* for a transplant programme\(^8\). The overriding aim of any transplant programme should be to minimise the donor organ and tissue shortage by optimising the levels of altruistic donation of organs and tissue and ensuring their allocation to the most clinically appropriate recipient. The system should be based on strict adherence to widely accepted ethical rules.\(^9\) Any practice contravening such principles is to be deprecated.

### 4.1.2. The six steps

The donation/transplant process should start with the identification (donor identification) of all individuals with brain death being ventilated in intensive care units (ICUs). Such potential donors should be carefully assessed to exclude contraindications to donation (donor screening) pending the necessary clinical and legal procedures required to establish and certify brain death. During this phase, the haemodynamic stability of the potential donor must be maintained (donor management) to preserve the viability of the organs. The legal or social requirements for authorising the removal of organs or tissues have to be met. The relatives will have to be approached and interviewed either to obtain formal consent or to obtain a social history about the potential donor. Adequate support for the family from trained staff at this time is essential. The existence of the donor has to be notified to a transplant co-ordinator or appropriate transplant organisation to ensure that an appropriately trained person takes charge of the process of organ removal. Arrangements, both within and outside the hospital, for (multiple) organ retrieval (and/or
tissue) must also be made. Organ retrieval, preparation, preservation and packaging preparatory to transportation are a difficult process, which requires significant expertise if organs are not to be damaged and rendered unusable. The organs retrieved should be allocated (organ allocation) according to previously agreed criteria preferably by an organisation, which holds a common waiting list and can co-ordinate the distribution and transport of organs. Organs will normally be transplanted within a few hours of retrieval, although kidneys can be stored for up to 24 hours. Many tissues may be stored for much longer periods but may require further processing.

The whole process can take many hours and involve a large number of staff with very different skills and from many backgrounds. Such a process cannot be left to chance. Protocols or operating procedures are needed for each step and the staff involved needs to be properly trained and adequately experienced in their respective roles. Even in the best centres with the most complete infrastructure, difficulties sometimes arise and there is a risk that either the donor or the organs will be lost. It is important to have a means of auditing the procedures to identify problems and modify procedures accordingly, if the continued effectiveness of the process is to be ensured. Ideally, one key (donor) person should be appointed in each area/hospital with the specific role of managing and monitoring the transplant process.

**Recommendation:** The transplant process is long and complex and cannot be left to chance. Protocols should be developed for each step and a key person should be made responsible in each area/hospital for managing and monitoring the process with the authority to determine where efforts and resources should be directed.

### 4.2. Donor detection: potential and identification

#### 4.2.1. Scope of the problem

Detecting potential donors is the starting point of transplantation and is possibly the most difficult to subject to standard protocols.
The only way to be sure that donors are not missed is to have a means of identifying and monitoring the potential and effective donor pools within relevant hospitals or areas. To do so requires collecting information about the total number of people certified as brain dead and the reasons, including relatives refusal, why some did not become donors. Reasons other than strict medical contraindications need to be examined including non-admission to an ICU. This in turn depends on the physicians in charge of patients identifying potential donors. The question remains how to monitor rates of potential and effective donation in such a way as to identify hospitals or areas where rates are low because of poor organisation or reluctance on the part of health care staff or relatives.

There are a number of possible indicators which depend on calculating rates of donation either in relation to the population of a specific area, or based on hospital indices such as the rate of donation compared to the hospital death rate, ICU death rate, or number of hospital beds, etc. The advantage of using indices based on large areas, e.g. a population of 10 million plus, is that rates are more reliable and stable over time. Data based on smaller populations or units may be affected by many factors.

Several studies using different methods suggest that rates of over 50 potential donors per million population per year (pmp/yr)\textsuperscript{(10-17)} can be achieved. None of the studies achieved 100% donor detection rates (Table I). Studies of hospital indexes\textsuperscript{(18-20)} have suggested that 2% to 3% of all people dying in a hospital and around 14% of those dying in the intensive care units, will suffer brain death. Of these, between 17% and 20% will have a medical contraindication to organ donation. Such studies suggest that rates of effective donation of well over 30 pmp/year, can be achieved. (Such rates cannot apply to all organs. Suitable donors for heart and lungs, for example, need to be younger and fitter). In contrast the mean organ donor rate in the European Union during 1995 was 14 donors pmp/yr. The cadaveric kidney transplant rate over the same period was 27.3 pmp/yr\textsuperscript{(1)}.
Such studies give an estimate of the possible “donor detection gap” between current donor rates and potential rates if this first step of donor detection were to be fully effective. It is, in theory, possible that in some countries the transplant rates could be more than doubled. However, it is difficult to extrapolate from such studies to provide expected local rates as these will vary due to local factors such as road death rates, intracranial haemorrhage prevalence, population density, number of ICU beds, age structure, etc.\(^{(21,22)}\) It is preferable to establish the donor detection gap for each hospital/area. Steps can then be taken locally to analyse the causes of the gap and implement measures to improve performance.

**Recommendation:** Published figures cannot be extrapolated to provide local rates of potential versus effective donors (although marked differences from published rates for potential donors should be considered as suggestive of under detection). The donor detection gap should be established for each hospital/area and systems for monitoring the rates established.

### 4.2.2. Improving donor detection

Knowledge of the environmental characteristics in the catchment area, e.g. health resources, infrastructure of the hospitals, location of neurosurgery teams and trauma centres, mortality rates, incidence of traffic accidents, cerebrovascular accidents, cerebral tumours, bullet wounds, etc. will help estimate the likely overall size of the donor detection pool. However, the best means of improving donor detection rates require an effective system for the early identification and follow up of all patients admitted to acute hospitals that may eventually be diagnosed as brain dead. The Donor Action Programme\(^{(23)}\) advises that information on potential brain death patients should be recorded prospectively but analysed retrospectively by means of a review of the medical record. This type of analysis will identify localities or hospitals with both an underdetection problem\(^{(17)}\) and failure to convert detected potential donors into effective donors.
Recommendation: A means should be developed to evaluate the size and characteristics of the potential donor pool to measure and monitor the potential donor rates. To ensure reliability, data should be collected prospectively and analysed retrospectively as recommended in the “Donor Action Programme”.

4.2.3. Donor detection programmes

The best means by which potential donors are detected and rates monitored is a proactive system of donor detection every acute hospital for which a person of sufficient authority is given responsibility. Ideally a key individual (key donation person) should be given the responsibility for:

i. development of a protocol for identifying potential donors which includes events to be recorded and clarifies the roles and responsibilities of hospital professionals in donor identification;

ii. educational programmes for health staff about transplantation;

iii. auditing donor procurement and problems on a regular basis.

Recommendation: Proactive donor detection programmes should be instituted in every acute hospital using specially trained professionals (key donation persons) working to agreed protocols and ethical rules.

4.2.4. The role of the “key donation person”

The key donation person needs to be a member of the hospital staff, well respected and closely related with the intensive care units. He/She should work in close relation, but independent from any transplant team(s) and report directly to the medical director of the institution and the OPO/OEO, who are accountable for overall performance. The role of the key donation person is now considered by many to be fundamental to improving donor detection rates. It is he/she who will be responsible for integrating the actions noted above; for development of donor detection programmes and specific protocols, etc., and for defining local benchmark figures and targets for improvement. The
appointment of such a person will make the difference between a successful and a non-successful donation programme.

**Recommendation:** A “key donation person”, independent from transplant teams, should be appointed in every acute hospital with clearly defines roles and responsibilities for establishing, managing and auditing systems for donor identification and identifying potential areas for improvement.

### 4.3. Donor screening: acceptability of organs

It is important to ensure that, as far as possible, any organs retrieved from a donor are of acceptable quality and do not pose an unacceptable risk to the recipient. The major risks to the recipient are the transmission of infectious or malignant disease with the organ. Advice on microbiological screening has been prepared by the Council of Europe\(^{(24)}\) and others and guidance on screening donors for malignancy has also been published by the Council of Europe.\(^{(25)}\) Standard protocols for screening potential donors should be developed locally.

The risk factors which determine the suitability of potential donors change from time to time and include not just the risk of transmission but the quality of the organ in terms of its viability. Improvement in donor management, organ preservation and transplant experience have meant that increasingly transplant teams can use organs which were considered marginal a few years ago.\(^{(26)}\) Protocols to assess the suitability of donor and each of their organs should be developed but will need to be reviewed from time to time to maintain the balance between minimising the risk of organ transplantation for the recipient and maximising the supply of organs.

**Recommendation:** Protocols should be developed setting out the criteria for screening potential donors and their organs for the risk of disease transmission and potential viability. All appropriate steps should be taken to avoid the transmission of infectious and neoplastic diseases and primary organ failure.
4.4. Donor management

4.4.1. Scope of the problem
There is time further to evaluate and screen the potential donor. After completing brain death certification, obtaining appropriate consent; fulfilling legal requirements (see below) and organising the retrieval procedure (see below), it is necessary to maintain the potential donor in a medical condition which will maximise the viability of the organs. Depending on time necessary to complete the above processes, donor management may be critical over a period of 24 hours or more during which time the donor’s condition could deteriorate sufficiently to prevent the use of some or all of the organs. Prevention of severe sepsis, maintenance of haemodynamic stability and avoidance of cardiac arrest are examples of good donor management. In a five-year study performed in a hospital in Barcelona, 14% (55/399) of otherwise acceptable organ donors suffered from either a cardiac arrest or uncontrolled sepsis which were contraindications to retrieval.\(^{(27)}\) In a Madrid study,\(^{(18)}\) 9.5% (107/1137) of all brain death subjects suffered a cardiac arrest at some point in the process. Similarly, a 1993 Basque study\(^{(16)}\) reported cardiac arrest in 11 of 131 potential donors (8.4%). In a multicentre Spanish audit performed during 1995, the figure had been reduced to 4%.\(^{(20)}\) In another study, an aggressive approach to donor management resulted in the transplantation of 44 donor hearts that might otherwise have been turned down.\(^{(28)}\)

4.4.2. Potential for improvement
The medical management of a potential donor is primarily the responsibility of the physician in charge of the ICU. However, at this stage the time for which such a doctor can be expected to keep and maintain a potential donor is limited, particularly given the pressure on ICU beds. Once death has been declared, donor management should transfer to the retrieval team leaving a potential gap. Therefore, the “key donor person” should also have responsibilities for donor management and particularly for overcoming problems, which can slow down the process.
The audit of potential donors, proposed in section 4.2 above, should also enable any complications arising in potential donors to be identified and analysed. Evidence of poor donor management which resulted in a loss of donated organs should be analysed and steps taken to avoid such complications in the future.

Research programmes into, and educational courses for, donor management have an important place improving our understanding of the problems and will help minimise the risk of complications, which will affect the acceptability of donors. New techniques or therapies that could help should be widely disseminated. Donor management training programmes for clinicians and nurses working with organ donors have proved very successful.\(^{(29)}\)

**Recommendation:** The incidence of irreversible cardiac arrest, sepsis and other contraindications to organ donation relating to donor management of potential donors should be monitored and audited to detect and correct any problems identified. Involvement of ICU staff in research and/or educational programmes on donor management should help raise standards.

### 4.5. Brain death

#### 4.5.1. Legal requirements

Most countries have laws or codes of practice that define the brain death. Ideally, the means by which brain death is established and certified and its relation to transplantation should be explicit and agreed nationally. However, there are still some countries, which do not have a comprehensive legal framework covering all aspects of transplantation. Countries are strongly advised to review, and where necessary enact, laws that should cover as a minimum:

i. an adequate definition of brain death which enables organ and tissue retrieval from donors after diagnosed brain death;

ii. the form of consent or authorisation required to enable organ and tissue donation;
iii. a requirement to register both the donor and recipient in such a way that donation is traceable but which maintains confidentiality;
iv. bans absolutely any form of trade in organs or tissues (organ trafficking);
v. the terms on which hospital staff and/or Health Authorities are permitted to retrieve and transplant the organs and tissues.

**Recommendation:** An appropriate legal framework for donation and transplantation is required which adequately defines brain death; the type of consent or authorisation required for retrieval (see below); the means of organ retrieval, traceability, confidentiality and which bans organ trafficking.

**4.5.2. Diagnosis and legal certification**

The clinical criteria to be met to establish a diagnosis of brain death are well recognised and accepted world-wide. They are discussed and explained in specialised publications. Where differences in practice exist, this is normally a result of the necessary legal criteria to be met in a particular country.

If there is any doubt about the cause of death, then a judge or a coroner must be informed. This requirement is not necessarily a bar to donation. Such deaths represent some 40% of all donations in Spain or the USA. The impact of judge's/coroner's practices on organ recovery has not been widely investigated but is thought to be variable. For example, between 1991 and 1994 in the Madrid region, judges refused organ removal from some 3.5% of all such cases. In the USA from 1990 to 1992 organs retrieval was refused in between 7% and 11.4% of coroner’s cases.

**4.5.3. Potential for improvement**

There are no internationally agreed criteria by which judges or coroners can decide in which cases it is appropriate to allow organ retrieval. Depending on the legal system and the nature of the suspect
death (e.g. trauma or sudden death versus suspected murder), some lawyers will see no reason to refuse organ removal whereas others may believe that it could prejudice full investigation, particularly in a suspicious death. It is advisable not just to keep such professionals fully informed about the benefits of transplantation, but to actively involve them in discussions about how best to minimise the loss of organs as a result of necessary legal procedures.

**Recommendation:** Law professionals should be fully aware of the transplant process and the co-operation of those most closely involved, i.e. judges and coroners, should be sought to reduce legal refusals to a minimum.

### 4.6. Authorisation or consent to organ donation

#### 4.6.1. Legal considerations

Most countries have laws relating to consent or authorisation required for organ and/or tissue donation for transplantation purposes. In many the consent of the relatives prior to organ procurement is required (Table II). However, (see below), there is a debate between authors about the relative merits of laws which presume consent (unless the individual has opted out) and those which require either the positive consent of the donor (via donor card or register) or the consent of relatives. Presumed consent laws, when fully accepted, seem to benefit donation, but, in practice, are often not applied mainly because of reluctance within the medical and legal communities to enforce donation. The King’s Fund Report did not recommend immediate implementation of presumed consent legislation in the UK on the basis that it could lead to public disagreement between professionals which would have an adverse impact on transplantation. If countries wish to apply a presumed consent law strictly, they need to develop a non-donor register which requires a significant infrastructure. Even then unfortunate misunderstandings are possible if the information about organ donation is not kept up to date or given out by untrained or under-trained staff.
In spite of the support organ donation receives in Spain, a recent survey showed that most people are against a change in current practice. Only 6% believed that organ removal should be performed without first consulting the wishes of the relatives.\textsuperscript{(34,35)} Reasons given by the general public in support of this attitude include the view that strict presumed consent represents an abuse of authority and/or that it is an offence against the relatives. Only one in five respondents to an UK survey in 1992 were in favour of the introduction of presumed consent whereas 50% were against the proposal.\textsuperscript{(21)}

In practice, because of the need to take a social history from available relatives, even in those countries with presumed consent laws, clinicians are reluctant to retrieve organs if the relatives object for fear of adverse publicity. It is essential that good records are kept of all consents or authorisations obtained for each donor.

**Recommendation:** It is advisable to ascertain the opinion of the public and health professionals about presumed or informed consent for organ donation before considering legal changes that might be potentially detrimental. The key donation person appointed in each centre/area must be aware of all local legal criteria and should be responsible for meeting these requirements. There should be a system for the safe custody of all certificates and test results required by the law.

### 4.6.2. Obtaining authorisation or consent

The approach to the relatives of a potential donor is another of the key steps in the transplant process and one of the most sensitive given that it necessarily coincides with the distress and trauma surrounding any death, particularly if that death is sudden or unexpected as is so often the case when the patient is young. Together with the initial identification of potential donors, refusal by relatives to consent to organ retrieval remains one of the major causes of loss of potential donor and a serious obstacle to improving organ donation rates.
4.6.3. Factors affecting willingness to allow organ donation

There is evidence\(^{19}\) that relatives will rarely refuse to allow organ donation if the donor has previously made clear his/her willingness to donate. A few people and/or their relatives will have strongly held beliefs, which will make them unwilling to donate organs under any circumstances. The majority of the people are “neither for or against” transplantation. The key questions are, therefore:

i. What factors will influence people to willingly agree to organ donation in advance and to make their wishes known to relatives and friends?

ii. What factors will influence relatives to agree to donation when the views of the potential donor are not known in advance? As noted above, although the legal position could, in theory, be a major factor, in practice it is not. The underlying public and professional attitudes to donation/transplantation are more important. One of the key factors influencing the willingness of individuals and their relatives to agree to organ donation, is the public attitude to transplantation at the time. Consideration should be given to how public and professional perceptions about transplantation can be positively influenced.

4.6.4. Public attitudes: impact of the media

As surveys have shown,\(^{21,35,36}\) there is significant public support for organ donation. One recent Spanish national survey shows a significant link between the public’s predisposition to organ donation and their view that transplantation is a “good” health care service. This suggests that bad publicity about important matters such as brain death, organ trafficking, or fairness of access to transplantation, can have an adverse effect on the public’s predisposition to agree to organ donation.

Many transplant professionals believe that adverse publicity about transplantation generates an increase in refusals to consent by lowering the image of transplantation among both the public and health care
workers not specifically involved in transplantation. The impact of positive or negative publicity is usually underestimated by the scientific community. There are some classic examples of negative effects. In 1980, after a prime time TV current affairs programme in the UK had questioned the validity of brain-death criteria (Panorama BBC), it took 15 months for donor referral rates to recover. France and Belgium, both countries with traditionally high organ donation rates, have recently experienced significant drops, attributed at least in part to negative publicity. In France it was revealed that there had been a failure to fully inform relatives of procurement procedures. In Belgium publicity was given to the high percentage of non-residents on national transplant waiting lists.

Rumours about organ trafficking (mainly false) have achieved the status of a “modern myth” probably because they embody some of the most potent fears about “science” in modern day life. Such rumours have caused significant damage to altruistic attitudes to organ donation all over the world.

In contrast, the so-called “Nicholas Green effect” is claimed to have had a positive effect on Italian public opinion with regards to organ donation. Nicholas was a 7-year old American child, shot dead by a bandit near Reggio Calabria in September 1994. His parents agreed to donate his organs after being asked to do so by Italian doctors. The Italian media reporting of the story – that the parents could still be generous to the Italian people in the face of the violence inflicted on their son – added to the positive impact of the parents’ decision on organ donation rates.

The media can have either a positive or negative influence on willingness to consent to donation. Journalists do not appear to deliberately promote or sensational stories about organ transplantation. Often they ask real questions about a complex and sensitive area but may report mistaken or imprecise answers. Such problems could be reduced by either better self control on the part of the media or better education of the media about transplantation issues (see below).
4.6.5. Communication strategies

There is no evidence that media stories, particularly the positive ones, have any long term effect on public attitudes to donation or on overall organ donation rates. This raises the question as to whether formal public education programmes can influence public attitudes to transplantation. In general, there is little evidence to suggest that direct publicity campaigns would influence the public unless resources comparable to the publicity budgets of major international companies are used. A television campaign conducted by the Department of Health in the UK showed a drop in the refusal rates from 30% to 22% during a period of intense publicity but it soon returned to precampaign levels.\(^{(21)}\) In 1987 an Australian national survey was undertaken to determine the population's knowledge about organ donation and transplantation. Two years later TV advertisements highlighting the need for organ donation were screened over a period of 6-12 months. A national follow-up survey in 1990 showed that knowledge about the next of kin's decision increased from 30% to 60%, but the percentage expressing a willingness to donate remained unchanged.\(^{(37)}\) There are no convincing reports from the medical literature, which support the idea that this type of approach can predispose people to organ donation.\(^{(21)}\) On the contrary, there is a growing feeling that such campaigns are ineffective or at least have a very high cost-effectiveness ratio.

During the last few years, attention has turned to trying to provide the media with accurate and positive information about organ donation and transplantation. In Spain, the Organisation National de Transplant (ONT) is responsible not only for co-ordination transplant services and providing guidance for the health care professions, but also for provision of information for the public and the media. Several strategies have been followed in an attempt to harness the power of the mass media and to improve the general level of information about these topics. The aims of these strategies are clearly defined:

i. to manage all potentially adverse publicity by trying to turn the media attitude to donation from negative to at least a receptive
and, if possible, a positive attitude towards organ donation and transplantation;
ii. creating a more positive atmosphere towards organ donation through the periodic dissemination of positive news.

The central messages to get over to the public have also been made very clear:

i. transplants are very effective and well-established procedures;
ii. they can offer long term survival and a high quality of life for increasing numbers of patients with no other hope of cure;
iii. organ donation is the only way to save such patients' lives;
iv. organ shortage is the main limitation to saving the live of more such patients;
v. any of us might need an organ.

In contrast there are negative messages which need to be countered. Organ transplantation should not be seen as:

i. an experimental procedure;
ii. a procedure whose main objective could be to benefit an individual surgeon, institution or any other form of self interest;
iii. a procedure only available for the wealthy or influential.

News or many kinds of programme, although not negative in themselves, can still pass on implicitly negative messages of this sort and need to be guarded against.

4.6.6. Target audiences

Given that the impact of public education is likely to be limited and also that the greatest potential for increasing the donor pool is detecting currently undetected donors, other types of education and/or communication might be more effective in increasing the supply of donors. The most important group which needs to receive adequate and appropriate information is health professionals, particularly
those responsible for identifying potential donors and/or approaching the grieving relatives. Most such health care professionals are not themselves involved directly in the transplant process and their knowledge of the success rates, etc. can be sparse. This group is also prone to being influenced by negative stories about transplantation.

It takes a special type of courage to discuss organ donation with shocked and distraught relatives and is not surprising, therefore, that health care staff put in such a position, are easily discouraged. Equally, the more such staff feel that what they are doing is beneficial and necessary, the more likely they are to be willing to try. The support of this group of health professionals is essential so that they should not just be the focus of communication strategies but should be directly involved in the development of such strategies to ensure that they have full confidence in the messages and are willing themselves to pass them on to other health care workers and the general public.

As noted above, another important target audience for any communication strategy is the media. Their influence on public opinion has already been discussed and it would be helpful to have the media generally better informed. One strategy being tried in Spain and Portugal is periodic meetings between journalists, experts in communications and leaders in the field of transplantation which are aimed at educating the media, addressing their misconceptions and emphasising the positive life-saving aspects of donation/transplantation.

4.6.7. Transplant “hotline”

Another information tool that has proved popular in some countries is a transplant hot line. Most comprise a single telephone number for a country or region, which is manned 24 hours/day, seven days/week, by trained staff who can provide relevant and accurate information rapidly. Originally intended for the public, such hotlines are popular with health care professionals, especially GPs, and the media. The fact that anyone, including the media, can, at any time, obtain medical, legal or statistical information about organ donation, has
helped reduce the incidence of adverse stories about transplantation, increased public confidence and helped generate a climate of trust and transparency about organ transplantation.

4.6.8. The need of professional support

Developing and managing an effective communications strategy is in itself a complex task. There are a number of elements for which either specialised training or the support of communications professionals are advisable. Training in communication and media skills is essential for those members of the transplant community who are highly visible and so likely to be approached by the media, and those who can and should act as spokespersons. Credibility is a major factor in good communications and it is helpful to be able to field representatives who can unhesitatingly produce positive messages.

Many transplant issues are either very delicate or complex. Some of the topics, e.g. brain death, organ trafficking, access to transplants, are controversial. If not handled correctly, they can have a catastrophic effect, at least in the short term, on organ donation rates. Professional advice should be sought on the best way to get over difficult messages. Again, help with the preparation of material, press releases, briefing packs, leaflets, etc., intended to explain such matters to the public and media. It may be helpful to issue to health professionals involved in transplantation with specific guidelines, which explain clearly and accurately such difficult topics to help them get effective messages to other health professionals, the public and the media.

Recommendations: Because both positive and negative messages can affect the public’s willingness to donate organs, there is a need for a professional attitude towards, and support from experts in, the field of communications. They should help to minimise the impact of “bad news” on, and to maximise the communication of “good news” about, transplantation to health professionals, the media and the public. Special attention should be paid to both the content of the message and the best means of dealing with the most controversial topics. The preparation of specific briefing materials should be considered.
The most cost effective means of increasing the publics willingness to donate seems to be improving the knowledge of health professionals (not directly involved in transplantation) and the media about transplantation issues. Continuing education should form an essential element of any communication strategy. A transplant hot line manned by appropriately trained professionals should be considered.

4.6.9. Approaching the relatives

The other major factor in reducing refusals when the wishes of the donor are not known is the manner in which the approach is made to the relatives at the time consent is sought. The high percentage of relatives refusing to agree to donation when the request is made has been noted. It is known that, when the wishes of the deceased are not known, only 50% of people will agree to organ retrieval from their relatives.\(^{35,36}\) One answer is to encourage people to speak about organ donation and transplantation and make their wishes known to their relatives. This could completely change the picture\(^{31,34}\) resulting in 93-94% of people allowing donation. But, as it is unlikely that the wishes of most people will be known, it is important to ascertain whether the attitude and skills of the staff in a position to seek agreement from relatives can influence their decision.

In the USA the Uniform Anatomical Gift Act 1987 contains a provision that requires staff to make routine enquiries of all potential donor’s relatives about organ donation. It provides that failure on the part of hospitals to adopt routine enquiry will lead to the denial of Medicare and Medicaid reimbursements. In spite of the requirements, it has been reported\(^{38}\) that up to 20% of potential donor families are not approached by the hospital staff. The reasons given include views of staff that donation can compound the family’s grief; there is a perceived conflict of interest, they are uneasy with the idea of donation itself or presenting the option to the relatives, or simply that staff lack of awareness of the process. The USA experience illustrates that simply to enact required request legislation is not enough. If you simply cite the law when asking relatives about organ donation the consent will be zero.\(^{39}\)
Analysis of the reasons for relatives refusing retrieval (Table III) do not vary very much from one country to another.\textsuperscript{(19,40,41)} In at least a proportion of the cases, the relatives’ decision could have been influenced by the way, in which the family was approached and informed. A large Spanish multicentre trial showed that an initial negative response can be changed into consent if the approach is right and the relatives doubts relate to brain death, the integrity of the corpse or religious causes. It is not so easy if the relatives have a negative attitude to transplantation or there have been problems with the hospital staff.\textsuperscript{(40)}

A study by the Partnership for Organ Donation\textsuperscript{(42)} and another Spanish study\textsuperscript{(43)} have demonstrated that bereaved families can also benefit from organ donation. The feelings of donor and non-donor families were studied one year after the death. Among donor families, 85\% in one study and 86\% in the other believe that donation provided a positive outcome of the death. Some 80\% said that donation helps the bereaved families, and 89\% or 100\% would donate again. Of the families that refused consent, 30\% in both studies would have changed their mind one-year later.

In many cases, the willingness or otherwise of relatives to agree to donation is not fixed but can be influenced by the attitude and skills of the health care staff who have to tell relatives bad news. It is essential that such staff are fully trained and experienced, not just in breaking the bad news of the donor’s death, but also in communicating the request for organ donation sensitively and being able to answer any doubts the relatives may have. Formal training should be mandatory for all such staff to give them the confidence to approach the relatives in the first place and to give them the best chance of obtaining a positive response. Contrary to the opinion of some authors, it seems that, if skilfully requested, agreement rates by relatives can be improved.\textsuperscript{(44-46)} or, at least, such training is not detrimental to organ donation.\textsuperscript{(47)} Some of the key attitudes include:

i.  we must realise that we are there to help and be useful and never to upset anyone;
ii. it is essential to make a comprehensive offer of help by trained staff who will continue to support the relatives independent of their decision;

iii. the first approach must be carefully prepared including learning about the family members/relatives; the time and place carefully considered and the request for organ donation separated from the communication of the death to allow the family the time necessary to accept the news;

iv. the relatives must not feel they are being hurried, for them there is no longer any need for speed;

v. it is advisable to continue to provide support and information to the family after donation.

Staff approaching grieving families should have been on specifically designed training programmes. Interviews should be carefully analysed in a follow up process by the responsible donation team to identify avoidable errors, e.g. not having provided adequate information; not following the rate of assimilation of concepts by the relatives; having lost control following some reactions, etc. Such routine evaluation helps determine and maintain best practice.

**Recommendation:** People should be encouraged to speak about organ donation and transplantation and to communicate their wishes to their relatives. As a donor’s wishes will not always be known, staff in a position to make requests for agreement to organ donation to relatives should be properly trained for the purpose. If such requests are well handled, the rate of donation refusals can be reduced.

**4.7. Organ retrieval**

**4.7.1. Introduction**

Once brain death has been established and the necessary consent or authorisation obtained, organ retrieval can take place. The age, condition and management of the donor will determine the number
of organs and tissue that can be retrieved. The retrieval procedure should be efficient and dignified so as to minimise the disruption to the donor hospital and staff. The key donation person or a transplant co-ordinator should be made responsible for making the arrangements including alerting the transplant centres to a possible donation early; providing donor data to a transplant centre or organ allocation organisation (see below) for identification of the most appropriate recipient; preparing for the retrieval team(s) and ensuring packing and transport is available for organs to be used in other centres. Procedures should be carefully planned, well rehearsed and regularly audited to ensure delays are kept to a minimum and that procedures are amended as necessary.

4.7.2. Multi-organ retrieval

A single donor can provide multiple organ and tissue donations (2 kidneys, heart, 2 lungs, liver, pancreas, small bowel, 2 corneas, heart valves, etc.). It is now recognised that as many organs as possible should be retrieved from each donor. Reported multi-organ donation rates vary from 30-80% but are improving. The latest report from the UKTSSA(48) shows an average of 3.5 organs retrieved per donor. However, organ transplant centres tend to be based on a single organ (kidney, liver and heart and lung). This has meant that specific organs have been retrieved by teams from different centres. Sometimes two or even three teams have arrived at the donor hospital each wanting to retrieve particular organs. This creates problems of timing as others may have to wait for the slowest team, prolongs retrieval times and risks one team damaging or affecting the viability of other organs. Such complex procedures can be distressing for the staff of the donor hospital making them less willing to participate in future organ donation.

Increasing use is being made of area or zonal retrieval teams with the skills and experience to retrieve several organs, preserve them and prepare them for transport to other centres. Appropriately trained teams can greatly improve the efficiency and dignity of the retrieval process. They arrive quickly and will often take a complete team
including anaesthetist and nursing staff so that staff of the donor hospital do not have to be involved in the retrieval. Countries should examine their retrieval methods and, where necessary, establish a retrieval system, which maximises multi-organ (and tissue) retrieval and minimises the length of the retrieval process and the disruption to the donor hospital.

4.7.3. Organ damage

There are very few reports of rates of organ damage during retrieval. However, recently there was sufficient concern about damaged kidneys in Finland to organise courses in retrieval training.\(^{(49)}\) Similarly a report to the UKTSSA Kidney Advisory Group in 1997\(^{(50)}\) showed that some 20% of kidneys were being damaged. Most were repaired and used but a further analysis of data for 1995-6 showed that approximately 1% of all organs (kidneys, hearts, lungs and livers) were not used because of damage during retrieval.\(^{(51)}\) In view of the organ shortage even the loss of one organ as a result of poor retrieval procedures is a matter for concern. All organ retrieval teams should be lead by a senior surgeon experienced in organ retrieval. Consideration should be given to ensuring that, as far as possible, all organs are retrieved by appropriately trained multi-organ retrieval teams. Organ damage should be reported and audited and, if necessary, further training provided. Regular training courses in organ retrieval should be provided for transplant surgeons in training. Finally, procedures for organ preservation, packaging and transport need to be well established and regularly reviewed. There is anecdotal evidence of organs being damaged e.g. by ice due to faulty packaging.

**Recommendation:** Organ retrieval procedures should be well planned to minimise delay and disruption to donor hospital. Retrieval teams should be lead by experienced surgeons trained, where appropriate in multi-organ retrieval. Organ damage during retrieval should be reported and monitored and further training provided as necessary to minimise damage during retrieval or transportation.
4.8. Organ allocation and organisational issues

4.8.1. Introduction
Given the short time (a few hours) that some organs (heart, lungs and liver) can be maintained in good condition prior to implantation, and the necessity to ensure that the organ is matched to a suitable recipient (size, blood group, HLA match, etc.), it is essential that effective systems are in place to ensure that the organs (and/or tissues) retrieved are allocated to the most appropriate patient(s). There should be at least a national patient waiting list with some form of co-ordinating office, covering a defined area which could be a region, country or even group of countries, in charge of all the organisational and administrative tasks necessary to ensure rapid and fair organ allocation. Every country should ensure there is in place a system which has transparent and justifiable organ allocation rules.

4.8.2. Organ allocation/exchange organisations
There is general agreement about the need for some sort of organisation to support transplant activity in a specific area, country or group of countries. Many such organisations already exist. Many are primarily organ sharing offices (OSOs) or Organ Exchange Organisations (OEOs) which were originally closely related to the tissue typing laboratories. The first and largest European organisations (Eurotransplant and France Transplant) had their origin and philosophy on HLA based kidney sharing during the sixties. They were created and developed as a result of professional agreements, which evolved further during the eighties to cover non-renal organs. However, such existing transplant organisations vary significantly from country to country in terms of:

i. scope – regional, national, supranational;
ii. size of population served – small < 10 m; medium 10-60 m; large > 60 m;
iii. management – professional; health administration; mixed;
iv. structure – non-for-profit foundation; state agency; private agency;
v. organisation – centralised/decentralised;
vi. objectives and responsibilities – organ sharing/exchange/procurement;

vii. activities – organs +/- tissues +/- bone marrow.

Such differences result from the origin and development of the organisation, the national health system of the country, the resources available and even the personal profiles of the founders and directors. Most such organisations world-wide are, however, dedicated at least to maintaining common patient waiting lists, agreeing and effecting organ sharing and allocation methods, registering donors and/or transplants, producing statistics and, in some cases, organising organ retrieval team arrangements.

**Recommendation:** An organ sharing/allocation organisation is essential but its roles and responsibilities must be clearly defined, particularly if it is to have a role in organ donation and procurement (see below).

### 4.9. Organisational support for transplantation

#### 4.9.1. Introduction

The preceding sections have covered the essential steps in transplantation and considered how the effectiveness of each step can be improved to maximise the procurement of high quality organs and their distribution to the most appropriate recipients. However, some sort of organisational framework is required to support, monitor and regulate not just organ allocation and exchange, but the whole process. This final section considers what support is required and how best it might be delivered.

#### 4.9.2. Hospital organisation

Starting at the beginning, the potential donors are to be found primarily in the ICU units of hospitals. There is a need to develop policies, which encourage hospitals to engage actively in organ donation. Such policies
should address the financial and other resource issues relating to organ donation. For example, the number of ICU beds, the facilities available for retrieval, the cost of maintaining patients on ICU, cumbersome brain death certification or organ retrieval procedures can, unless addressed, all inhibit a hospital from seeking to maximise organ donation.

**Recommendation**: Attention should be paid to ensuring that hospitals are properly resourced and, if necessary, reimbursed for maximising organ procurement.

**4.9.3. Organ procurement organisation**

There is no single formula for an appropriate supra hospital organisation that can ensure good results. It is increasingly argued that the ideal situation is an integrated organisation that can support the whole process of organ donation and allocation (see below). There is, however, an apparent contradiction, which must be recognised because it has implications for the optimum size and type of organisation. As far as organ sharing is concerned, and with some limitations (time, cost), it has been accepted that “the larger the pool of patients, the better the match.” (52) Suitable organs cannot easily be found for urgent patients and “difficult” recipients (children, highly sensitised renal patients, and rare HLA types) within the scope of a small organisation. Such considerations point to a large organisation as the optimum model.

However, when it comes to maximising organ donation, there are data, which indicate the opposite is true, i.e. that smaller organisations are more effective than the bigger ones. (53) This is thought to be due to a better knowledge of local factors, knowing and being able to influence the professionals involved and more direct accountability for the whole process. Large centralised organisations whose staff do not fully participate in the decision making process are generally strongly de-motivating and so would not readily promote increased organ donation. Moreover, there are those who would argue strongly that cadaveric organs procured within a community should be considered assets of the community and that the community rather than just the medical profession should determine their allocation through agreed criteria. (54)
Recommendation: In order to optimise organ donation there is need for a supra hospital transplant organisation, appropriate in size and structure to the local situation with specific responsibilities for the whole process of organ procurement.

4.9.4. Transplant support: organisational objectives

Ideally, any transplant-co-ordinating organisation should fulfil two fundamental functions. It should provide overall support for the donation/transplant process and be in direct charge of distributing organs with all that entails. Such an organisation would not be an OPO or OSO, i.e. concerned only with organ sharing, but have a clear objective of maximising the supply of donor organs. Such an organisation should be able to detect any problem, which could lead to a loss of donors, and offer solutions. This would only be possible if the organisation could develop well established protocols covering the whole process described above, audit the results of hospitals or local organisations through effective data analysis, promote relevant research, provide training programmes and supply accurate and appropriate information.

The organisation would be responsible for ensuring the legal and ethical acceptability of the donation process and be able to guarantee the fairness and transparency of both organ allocation criteria and the equity of access of all recipients. The organisation should also be responsible for organ (and tissue) exchange between it and other recognised national or supranational organ transplant co-ordinating organisations. In summary, the organisation should be able to agree and implement operational policies covering all aspects of the donation/transplant process.

4.9.5. Transplant support organisations

The question then arises as to whether there are any existing examples of organisations which have attempted to combine the benefits of smaller local organisations directed to organ procurement with those of the large, possibly multinational OEO? As has been noted above, there are
in Europe (and elsewhere) a number of large transplant organisations, which vary in their roles and responsibilities, Eurotransplant, France Transplant, Scandia Transplant, ONT, and the UKTSSA. The UKTSSA maintains a common waiting list and is responsible for organ allocation, but has also agreed protocols for organ retrieval. Three years ago, it introduced zoning arrangements throughout the UK to improve organ retrieval and distribution. In Spain, ONT is implementing a system of interdependence between district/regional based procurement arrangements which work as part of a national transplant organisation. The type of organisational solution, which seems to be the most appropriate, is one which offers the possibility of ensuring a common approach and standards with sufficient local autonomy to maintain enthusiasm.

**Recommendation:** The most effective organisational approach balances the requirements for effective organ procurement (small/local) with those for organ allocation (large, national/multinational). The aim should be to optimise organ procurement whilst ensuring the most clinically effective allocation of organs and tissues.

### 4.9.6. National responsibilities

Whatever organisation is established, the direct, or at least indirect involvement, of national health administrations in the transplant system is essential to provide the necessary legal framework and resources and to guarantee that someone is held accountable for the performance of the transplant service and the safety and traceability of the organs and tissues donated.

**Recommendation:** Health Administrations are responsible for ensuring that there is proper organisational support for organ donation and distribution and should guarantee the fairness, transparency and safety of the whole system.
5. International co-operation

The majority of organs retrieved will be used either in the same region or within a country of organ transplant organisation, but some international exchange of organs is desirable either for urgent cases (livers) or difficult tissue matches (kidneys, bone marrow). It is important that the clinicians using such organs can feel confident in the screening and retrieval systems in the donor country. The organisation of organ retrieval systems will be regional and/or national and be adapted to best meet local health service organisation and legal framework. Again, however, it is desirable that such systems achieve some common standards. Bad publicity about organ transplantation in one country may have an impact on organ donor rates in others. Patients may try to get put on waiting lists in different countries. There is, therefore, a common interest in ensuring that transplant services are, and are seen to be, above reproach. Organisations may have much to learn from each other about solutions to problems and cost effective organisation.

Such co-operation should be established and may be achieved either by international agreement or by some sort of supranational organisation.

The following aspects of the organ donation/transplantation process might be the subject of such international co-operation:

i. learning, exchange of experience;
ii. training of people involved in organ donation;
iii. prevention of commercialisation;
iv. validation of waiting lists;
v. finding organs for “problem” recipient;
vi. tracing of organs form donor to recipient;

vii. accountability and transparency or transplantation services;

viii. standardisation and/or accreditation of e.g. hospitals, laboratories and transplantation services;

ix. educating and informing the population and the media.

**Recommendation:** International co-operation on the promotion of organ donation is desirable to maximise organ donation and equalise access to transplantation between countries. Governments should actively promote such co-operation.

**Recommendation:** Priority should be given to international co-operation which improves standards of training, exchange of experience, and which helps guarantee the safety of organs and the ethical standards by which they are retrieved and transplanted.

**Table I. Potential organ donation rates and effectiveness in donor detection in different countries/areas**

<table>
<thead>
<tr>
<th>Year</th>
<th>Potential donor pool (donors pmp/year)</th>
<th>Donor detection effectiveness rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>50.8</td>
<td>75%</td>
</tr>
<tr>
<td>Siminof et al. Pennsylvania + Minnesota (11) 1995</td>
<td>1991-92</td>
<td>65.4(*)</td>
</tr>
<tr>
<td>Nathan et al. Pennsylvania (12) 1991</td>
<td>1987</td>
<td>38.3-55.2</td>
</tr>
<tr>
<td>Espinel et al. Cataluña (13) 1989</td>
<td>1987</td>
<td>40</td>
</tr>
<tr>
<td>Aranzabal et al. Euskadi (14) 1995</td>
<td>1993</td>
<td>53</td>
</tr>
<tr>
<td>Evans et al. Usa (15) 1992</td>
<td>—</td>
<td>43.7</td>
</tr>
<tr>
<td>Multicentre Spanish study (16) 1994</td>
<td>1994</td>
<td>65 (*)</td>
</tr>
</tbody>
</table>

*Brain dead declared people medical contra-indications including ( ) = References
Table II. The type of consent required in different countries

<table>
<thead>
<tr>
<th>Presumed consent</th>
<th>Theoretically presumed consent but practically informed consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>Spain</td>
</tr>
<tr>
<td>Portugal</td>
<td>Italy</td>
</tr>
<tr>
<td>Austria</td>
<td>Greece</td>
</tr>
<tr>
<td>Sweden</td>
<td>Belgium</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Luxembourg</td>
</tr>
<tr>
<td>Slovak Republic</td>
<td>France</td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
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<tr>
<td>Poland</td>
<td></td>
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<tr>
<td>Spain</td>
<td></td>
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<tr>
<td>Portugal</td>
<td></td>
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<tr>
<td>Austria</td>
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<tr>
<td>Spain</td>
<td></td>
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<tr>
<td>Austria</td>
<td></td>
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<tr>
<td>Portugal</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td></td>
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<tr>
<td>Latin America</td>
<td></td>
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<tr>
<td>United Kingdom</td>
<td></td>
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<tr>
<td>Ireland</td>
<td></td>
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<tr>
<td>Denmark</td>
<td></td>
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<tr>
<td>Netherlands</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td>Informed consent</td>
<td>No legislation. Practically: informed consent</td>
</tr>
<tr>
<td>USA</td>
<td></td>
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<tr>
<td>Latin America</td>
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<tr>
<td>Netherlands</td>
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<tr>
<td>Germany</td>
<td></td>
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Table III. Reasons for refusal by country

<table>
<thead>
<tr>
<th>Reasons for refusal</th>
<th>Spain</th>
<th>France</th>
<th>Spain (Madrid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centres</td>
<td>12</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Interviews</td>
<td>618</td>
<td>213</td>
<td>352</td>
</tr>
<tr>
<td>Refusal Rate</td>
<td>16.6</td>
<td>26</td>
<td>25.2</td>
</tr>
<tr>
<td>Reference</td>
<td>(30)</td>
<td>(32)</td>
<td>(17)</td>
</tr>
<tr>
<td>Lack of/ Inaccurate information provided to the family</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Brain Death</td>
<td>5.8%</td>
<td>22%</td>
<td>9%</td>
</tr>
<tr>
<td>– Corpse Integrity</td>
<td>4.8%</td>
<td></td>
<td>5%</td>
</tr>
<tr>
<td>Family opposed</td>
<td>24.2%</td>
<td>32.3%</td>
<td>25%</td>
</tr>
<tr>
<td>Lack of information about donors wishes</td>
<td>3.8%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Social claims</td>
<td>3.8%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Negative attitude of the deceased during his/her life</td>
<td>40%</td>
<td>36.7%</td>
<td>38%</td>
</tr>
<tr>
<td>Religious reasons</td>
<td>2.9%</td>
<td></td>
<td>7%</td>
</tr>
<tr>
<td>Problems with hospital staff</td>
<td>7.7%</td>
<td>9%</td>
<td>12%</td>
</tr>
</tbody>
</table>
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Executive summary of the Joint Council of Europe/United Nations Study on trafficking in organs, tissues and cells and trafficking in human beings for the purpose of the removal of organs

In 2008, the Council of Europe and the United Nations agreed to prepare a Joint Study on trafficking in organs, tissues and cells and trafficking in human beings for the purpose of the removal of organs. This Joint Study was prepared in the framework of the co-operation between the two international intergovernmental organisations, in particular in keeping with the United Nations General Assembly Resolution on Co-operation between the United Nations and the Council of Europe (A/RES/63/14), which specifically states:

“[The General Assembly] Takes note with appreciation of the entry into force on 1 February 2008 of the Council of Europe Convention on Action against Trafficking in Human Beings, to which any non-member State of the Council of Europe may accede after having obtained unanimous consent of the parties to the Convention, commends the enhanced co-operation between the United Nations and the Council of Europe in this regard, and expresses its appreciation for the preparation of a joint study on trafficking in organs, tissues and cells and trafficking in persons for the purpose of the removal of organs”.
The Study notes, first of all, that trafficking in human beings for the purpose of organ removal is a small part of the bigger problem of trafficking in organs, tissues and cells (“OTC”). Secondly, it highlights the existence of widespread confusion in the legal and scientific community between “trafficking in OTC” and “trafficking in human beings for the purpose of the removal of organs”. Thirdly, the Joint Study underlines that solutions for preventing the two types of trafficking had to be different because the “trafficked objects” are different: in one case the “organs, tissues and cells” and in the other case the “person him/herself” who is trafficked for the specific purpose of removing his/her organs. One of the major aims of the Joint Study is therefore to distinguish between trafficking in OTC and trafficking in human beings for the purpose of organ removal.

The Joint Study only covers trafficking in OTC for the purpose of transplantation. Other purposes of trafficking in OTC are outside the scope of the Joint Study. The starting point of the Joint Study is the prohibition of making financial gains with the human body or its parts. This principle was established for the first time in a legally binding instrument in Article 21 of the 1997 Council of Europe Convention on Human Rights and Biomedicine [CETS No. 164]: “The human body and its parts shall not, as such, give rise to financial gain”. The principle was then reaffirmed in the 2002 Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin [CETS No. 186]. Article 22 of the Protocol states: “Organ and tissue trafficking shall be prohibited”. The principle of the prohibition of making financial gains with the human body is also very important in order not to jeopardise the donation system based on altruism, both from living and from deceased donors, which must be the basis of the organ transplantation system. Given that trafficking in organs mainly exists because of the lack of available organs, it is also essential to take the organisational measures needed to increase the availability of organs for transplantation.

Taking into account the above-mentioned considerations, the main conclusions and recommendations of the Joint Study can be summarised as follows:
– The need to distinguish clearly between “Trafficking in OTC” and “Trafficking in human beings for the purpose of the removal of organs”. The two are frequently confused in public debate and in the legal and scientific community. This leads to general confusion and consequently hinders effective efforts to combat them and also to provide comprehensive victim protection and assistance.

– The principle of the prohibition of making financial gains with the human body or its parts should be the paramount consideration in relation to organ transplantation. All national legislation concerning organ transplantation should conform to this principle.

– The need to promote organ donation and establish organisational measures to increase organ availability. Preference should be given to deceased organ donation, which should be developed to its maximum therapeutic potential. In addition, there is a need to extend worldwide the organisational and technical capacity for the transplantation of organs.

– The need to collect reliable data on trafficking in OTC and on trafficking in human beings for the purpose of organ removal. There is limited knowledge of the two issues since little information is available from official sources. The information about the number of victims and trafficked OTC therefore remains rather fragmentary. This hinders both the quantification of the two and also their qualitative description. The data should be disaggregated by sex in order to assess whether and to what extent the processes disproportionately affect women and girls. States should make efforts in terms of data collection in relation to both problems.

– The need for an internationally agreed definition of “Trafficking in organs, tissues and cells”. This Joint Study did not aim to provide a definition of “Trafficking in OTC”. Such a definition should be agreed upon at international level with the involvement of all the relevant players. While underlining that all national systems should be based on the principle of the prohibition of making financial gains with the human body or its parts, the starting point for such a definition should be the idea that any organ transaction outside
the national systems for organ transplantation should be considered organ trafficking. It is therefore recommended that an international legal instrument be prepared, setting out a definition of “Trafficking in OTC” and the measures to prevent such trafficking and protect the victims, as well as the criminal-law measures to punish the crime.

- “Trafficking in human beings for the purpose of the removal of organs” is included in the definition of trafficking in human beings in the Council of Europe Convention on Action against Trafficking in Human Beings [CETS No. 197] and in the United Nations Protocol to Prevent, Suppress and Punish Trafficking in Persons, especially Women and Children, Supplementing the United Nations Convention against Transnational Organised Crime. Indeed, the definition of trafficking in human beings set out in both legal instruments explicitly states that exploitation also includes the removal of organs. The principles and measures applicable to other forms of exploitation of trafficking in human beings must also be applied to combat this type of trafficking for organ removal. There is no need for the further development of a legally binding international instrument at universal or regional level. All relevant aspects for preventing and combating trafficking in human beings for organ removal are set out in the above-mentioned legally binding international instruments.