Guide to safety and quality assurance for organs, tissues and cells

3rd edition: 2006 version

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISCUSSION AND REVISION OF THE 2nd EDITION BY COMMITTEE OF EXPERTS ON SAFETY AND QUALITY ASSURANCE FOR ORGANS, TISSUES AND CELLS (SP-S-QA)</td>
<td>4-7 APRIL 2005</td>
</tr>
<tr>
<td>APPROVAL OF 1st DRAFT OF THE 3rd EDITION BY THE COMMITTEE OF EXPERTS ON ORGANISATIONAL ASPECTS OF CO-OPERATION IN ORGAN TRANSPLANTATION (SP-CTO)</td>
<td>14-15 APRIL 2005</td>
</tr>
<tr>
<td>RELEASE OF DRAFT OF THE 3rd EDITION FOR CONSULTATION</td>
<td>1 JUNE 2005</td>
</tr>
<tr>
<td>CONSULTATION PERIOD – COMMENTS REQUESTED BEFORE</td>
<td>30 NOVEMBER 2005</td>
</tr>
<tr>
<td>EXAMINATION OF COMMENTS AND RELEASE OF DRAFT 3rd EDITION OF THE GUIDE</td>
<td>APRIL 2006</td>
</tr>
<tr>
<td>ADOPTION OF FINAL 3rd EDITION BY SP-CTO</td>
<td>APRIL 2006</td>
</tr>
<tr>
<td>APPROVAL OF 2006 VERSION BY THE EUROPEAN HEALTH COMMITTEE (CDSP)</td>
<td>JUNE 2006</td>
</tr>
<tr>
<td>PUBLICATION OF THE 3rd EDITION OF THE GUIDE</td>
<td>AUGUST 2006</td>
</tr>
</tbody>
</table>

Secretariat note: For the first version: additions to the second edition of the Guide are in **bold italics** and deletions are struck out.
Guide to safety and quality assurance for organs, tissues and cells

3rd edition

DRAFT

Council of Europe Publishing
French version:

*Guide sur la sécurité et l’assurance de qualité des organes, tissus et cellules*

ISBN 92-871-5517-8

*All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic (CD-Rom, Internet, etc.) or mechanical, including photocopying, recording or any information storage or retrieval system, without prior permission in writing from the Publishing Division, Communication and Research Directorate.*

Cover: Rostyslav Hlukhovetsky
Layout: DTP Unit, Council of Europe
Edited by Council of Europe Publishing
http://book.coe.int

Council of Europe Publishing
F-67075 Strasbourg Cedex

ISBN 92-871-5518-6
© Council of Europe, September 2004
Printed in Belgium
# CONTENTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CHAPTER 1 – INTRODUCTION</strong></td>
<td></td>
</tr>
<tr>
<td>1.1 Introduction and Scope</td>
<td>7</td>
</tr>
<tr>
<td>1.2 Benefits of transplantation</td>
<td>9</td>
</tr>
<tr>
<td>1.3 Risks of transplantation</td>
<td>10</td>
</tr>
<tr>
<td>1.4 Ethical issues</td>
<td>12</td>
</tr>
<tr>
<td>1.5 Quality management</td>
<td>13</td>
</tr>
<tr>
<td>1.6 Organisational issues</td>
<td>13</td>
</tr>
<tr>
<td><strong>CHAPTER 2 – QUALITY MANAGEMENT: PRINCIPLES FOR ENSURING THE</strong></td>
<td></td>
</tr>
<tr>
<td>2.1 Introduction</td>
<td>17</td>
</tr>
<tr>
<td>2.2 General principles</td>
<td>17</td>
</tr>
<tr>
<td>2.3 Examples of quality management systems</td>
<td>17</td>
</tr>
<tr>
<td>2.4 Terminology</td>
<td>18</td>
</tr>
<tr>
<td>2.5 Basic requirements</td>
<td>19</td>
</tr>
<tr>
<td>2.6 Quality management</td>
<td>19</td>
</tr>
<tr>
<td><strong>CHAPTER 3 – SELECTION OF DONORS</strong></td>
<td></td>
</tr>
<tr>
<td>3.1 General requirements</td>
<td>29</td>
</tr>
<tr>
<td>3.2 Deceased donors</td>
<td>29</td>
</tr>
<tr>
<td>3.3 Living donors</td>
<td>46</td>
</tr>
<tr>
<td>3.4 Collection of surgical residues</td>
<td>52</td>
</tr>
<tr>
<td>3.5 Re-testing of living donors of stored allogeneic material</td>
<td>52</td>
</tr>
<tr>
<td><strong>CHAPTER 4 – ORGAN PROCUREMENT AND PRESERVATION</strong></td>
<td></td>
</tr>
<tr>
<td>4.1 Deceased donors</td>
<td>53</td>
</tr>
<tr>
<td>4.2 Living donation</td>
<td>55</td>
</tr>
<tr>
<td>4.3 Organ preservation, packaging, transportation and traceability</td>
<td>56</td>
</tr>
</tbody>
</table>
# Chapter 5 – Tissue and Cell Procurement

- **5.1 Procurement from Deceased Donors** ................................................................. 59
- **5.2 Procurement from Living Donors** ................................................................. 60
- **5.3 Donor Identification** ....................................................................................... 60
- **5.4 Donor Identification Number** ......................................................................... 60
- **5.5 Labelling and Packaging** ............................................................................... 61
- **5.6 Procurement Documentation** .......................................................................... 62
- **5.7 Storage and Transportation to Processing Facility** .......................................... 62
- **5.8 Haematopoietic Progenitor Cells (HPC): Specific Issues** ............................... 63

# Chapter 6 – Tissue Establishments

- **6.1 General Organisational Requirements of a Tissue Establishment (TE)** .......... 65
- **6.2 Facilities and Equipment** ................................................................................. 68
- **6.3 Tissue and Cell Processing, Preservation and Storage** .................................. 71
- **6.4 Release of Tissue or Cells** ................................................................................ 78
- **6.5 Distribution** .................................................................................................... 78
- **6.6 Traceability** ..................................................................................................... 79
- **6.7 Transportation** ................................................................................................ 79
- **6.8 Return into Inventory** ..................................................................................... 79
- **6.9 Exceptional Release Appendices** .................................................................... 79
- **6.10 Recipient Adverse Events and Non-Conformances** ..................................... 80
- **6.11 Hospital Tissue and Cell Storage and Distribution** ....................................... 81

# Chapter 7 – Transplantation Practices

- **7.1 Organisational Issues** ..................................................................................... 83
- **7.2 Pre-Transplant Period** .................................................................................... 83
- **7.3 Peri-Transplant Period** .................................................................................. 87
- **7.4 Post-Transplant Period** .................................................................................. 88
- **7.5 Use of Organs, Tissues and Cells for Purposes Other Than Transplantation** .... 90

# Appendix 1 – SP-SQA Group Participants

# Appendix 2 – List of Relevant Standards/Guidelines

# Appendix 3 – Example of the Evaluation of Donor Risk Factors for
1  TRANSMISSIBLE DISEASES .................................................................101
2  APPENDIX 4 – DEFINITIONS .............................................................103
3  APPENDIX 5 – ADDITIONAL PROTOCOL TO THE CONVENTION ON HUMAN RIGHTS AND BIOMEDICINE, ON TRANSPLANTATION OF ORGANS AND TISSUES OF HUMAN ORIGIN .................................................................109
Chapter 1 – Introduction

1.1 Introduction and scope

In 1999, the European Health Committee (CDSP) of the Council of Europe set up a working group to prepare guidance on the standards required and the quality assurance that should be achieved in services for the transplantation of human organs, tissues and cells in member states, resulting in this guide. The first edition was published in 2002. It was then decided to set up a Group of Specialists (SP-SQA) to update the guide every 2 years. The group worked on the second edition during 2003-04. The work on the third edition started in 2005. In the meantime, the European Union adopted a Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. The Council of Europe and the European Commission will co-operate to ensure that the standards set under the directive are compatible with the guide and that the same standards are applied throughout Europe.

The purpose of this document is to provide guidance for all those involved in the transplantation and other clinical application of organs, tissues and cells to optimise their quality (and thereby the rate of success of transplants) and minimise the risks of these complex procedures.

This guide includes safety and quality assurance standards for procurement, preservation, processing and distribution for organs, tissues and cells of human origin (allogeneic and autologous) used for transplantation purposes. The following is a non-exhaustive list of what is covered in the guide:

- solid organs including kidney, liver, heart, lung, pancreas and small bowel;
- all tissues such as bone, tendons, skin, corneas, cardiovascular tissues, foetal membranes and others; used for transplantation purposes, including surgical residues;
- cells from all human sources including haematopoietic progenitor cells (HPC) from all sources and cells for cellular immune therapies (CIT);
- embryonic and foetal tissue;
• surgical residues.

Organs, tissues and cells not covered by this document include:

• gametes;

• blood and blood products (*as defined in and covered by the CoE Guide on blood components*);

• genetically modified human material (*see Directive 2003/63/EC. Part IV Advanced Therapy Medicinal Products*).

Procurement of dura mater for transplantation is not recommended, and it is forbidden in many countries due to the risk of prion transmission.

This document applies to the transplantation of organs, tissues and cells of human origin transplanted into persons for therapeutic purposes. The terms used in this document are defined in Appendix 4.

*Genetically modified human materials are considered to be medicinal products (EU Directive 2004/27/EC on medicinal products) and additional requirements apply which are not included in this Guide. Specific guidelines on these requirements have been published by the EMEA/CPMP will deal with genetically modified human material and will define, in particular, the conditions under which the present guidelines will be applicable, as a whole or in part.*

While embryonic stem cells do fall within the scope of this document their application is currently restricted to clinical trials. It is recommended, wherever practical, that these activities be governed by quality systems to ensure their safety. No specific recommendations are therefore included in this edition of the guide. The ethical issues surrounding this and other foetal-derived tissue should be addressed by the member states of the Council of Europe.

The general bioethical principles to be respected are laid down in the Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and
Tissues of Human Origin, formally approved by the Committee of Ministers on 24 January 2002 (see Appendix 5).

### 1.2 Benefits of transplantation

Organ transplantation is now the most cost-effective treatment for end-stage renal failure, and it is the only available treatment for end-stage failure of organs such as the liver, lung, and heart. Risk:benefit analysis is thus of major importance.

Transplantations of tissues such as corneas, cardiovascular tissues, bone, tendons and skin are all well-established therapeutic techniques. Although not all of these tissues are necessarily lifesaving, such transplants nevertheless offer major therapeutic benefits to a wide range of patients.

The demand for bone transplantation is increasing very rapidly, particularly for secondary revision of hip replacement operations. Demand for skin for treatment of burns has also increased.

Cell transplantation, for example haematopoietic progenitor cell (HPC) bone marrow (BM) transplantation, is also well established and can be lifesaving in the treatment of severe immunodeficiency syndromes and many types of haematological malignancy—and is now used to treat some autoimmune diseases.

Interest in other types of cell transplantation is also rapidly growing (e.g. transplantation of pancreatic islet cells). It is now possible if in the future, it becomes feasible to replicate, or to expand, and cells in vitro, or to genetically modify them—cells in vitro—to overcome inherited defects, then cell transplantation will be a new treatment modality. New CIT are being developed with a potential to treat viral, malignant, and autoimmune diseases, and for inducing tolerance. In addition, there are some products that incorporate human cells in synthetic matrices: the safety and quality of the originating human cells should be assured e.g. to prevent disease transmission.
Successful transplantation, even when not lifesaving, offers recipients major improvements in their quality of life. Life with a kidney transplant has been shown to be preferable to life on dialysis. Restoration of sight with cornea transplantation or of mobility using allograft bone in revision hip replacement surgery, and the replacement of heart valves, removing the need for long-term anticoagulation, offer major benefits to the recipient.

1.3 Risks of transplantation

Transplantation, whether of organs, tissues or cells, is not without some risk to the living donor, the recipient, and the health care professionals involved.

Transplantation carries the risk of the operative procedure itself and, for example, of the lifelong immunosuppression necessary in organ transplantation. In each case the potential benefits of the transplant procedure should outweigh the risks. The factors influencing the clinical outcome of transplantation are complex and there is an interaction between two different biological systems, that of the donor and the recipient. Therefore when assessing the risk of transplantation, aspects of both donor and recipient should be considered. In each case the potential benefits of the transplant procedure should outweigh the risks (see also 2.6.5).

1.3.1 Donor

Living donors of organs, tissues or cells will face risks associated both with testing to ascertain their suitability as a donor and the procedure to obtain the organ, tissue or cells. Complications may include medical, surgical, social, financial or psychological problems and, in the worst case scenario, could seriously incapacitate the donor or even lead to the donor’s death. As donors are volunteers and otherwise healthy individuals, all possible measures must be taken to minimise the risks to the donor. In most cases of removal of surgical residues, there is no additional risk for the donor. If, however, procurement does result in additional risks for the donor, the donor has to give informed consent concerning these risks. Procurement can result in additional risks to the donor, and such information should be provided (see also 3.3.2).
1.3.2 Recipient

In most circumstances, the major risk to the transplant candidate is failure to obtain transplantation through, for example, organ shortage.

Other risks for the recipient may include:

- failure of the transplant because the graft is inadequate, damaged or poorly preserved and fails to function (primary graft failure);
- risks associated with the transplantation procedure;
- rejection of organs, tissues or cells, either acutely or over the longer term (chronic rejection);
- disease transmission such as an infection or a malignancy;
- contamination or damage of the graft in some other way during transport, processing or storage;
- complications of immunosuppression and other concomitant therapies;
- recurrence of primary disease.

To minimise the risks to the recipient, it is essential to screen donors and establish the presence or absence of disease transmission risk in their organs and tissues. **Informed consent should be obtained from all recipients (or their legal representatives). This should document relevant risks taking into account individual circumstances.** A patient may be willing to risk becoming infected by a donor known to have hepatitis, for example, if the choice is between life with infection or death. Scarce organs, tissues and cells which carry a specific risk should not be rejected out of hand but offered in case there is someone who could benefit. However, the transplantation of materials from a high risk donor for non-life-threatening conditions cannot be justified.
1.3.3 Health care workers

Transplantation procedures can result in the infection of health care professionals involved in the donation or transplant process. Testing, prophylactic measures for transmissible agents and regular follow-up should be available for all health care workers involved in transplantation.

1.4 Ethical issues

It is essential for practice to be in line with the Additional Protocol to the Convention on Human Rights and Biomedicine, on Transplantation of Organs and Tissues of Human Origin, and the Council of Europe’s Resolution (78) 29 on harmonisation of legislation of member states relating to removal, grafting and transplantation of human substances to ensure that all aspects of organ transplantation, tissue and cell banking and transplantation conform to ethical standards.

Any intervention in the field of organ, tissue and cell transplantation should be carried out in accordance with relevant professional obligations and standards.

1.4.1 Altruistic donation

The use of material derived from one human being for the treatment of others poses major ethical questions for those individuals and the societies in which they live. The human body and its parts should not, as such, give rise to financial gain or comparable advantage. It is now widely accepted that organs, tissues and cells should be donated, and not be the subject of commercial gain. Such donations, whether by living donors or from deceased persons, should be altruistic. The principle of altruistic donation has been enshrined in a number of legal instruments. In some countries organ donations by unrelated living donors are restricted.

1.4.2 Protection against abuse

The current demand, particularly for organs but to a lesser extent for some tissues, far outweighs the supply. Because transplantation is effective the demand will remain high and
under such circumstances it is essential to ensure that both donors and recipients have adequate protection against exploitation and the inevitable risks associated with complex procedures. For a donor who is a minor, informed consent must be obtained from the donor, but in accordance with applicable law also from the donor’s parents, legal guardian or from a court. Informed consents should be documented. International agreements and national law should set the framework within which organ, tissue and cell transplantation operate in each country. In particular, they should set out protocols for establishing death, *information given (risks and benefits)* and the consent and authorisation needed to remove organs, tissues and cells for transplantation and the way organs, tissues and cells are allocated.

1.5 Quality management

In order to reduce the risk and maximise the benefits of the transplantation process, it is necessary to operate an effective quality management system (QMS). Quality systems are discussed in Chapter 2.

1.6 Organisational issues

The retrieval and distribution of organs, tissues and cells should be properly regulated. Whether the material is to be used for therapeutic, research or other purposes, it is important that those receiving or using the material have confidence in the quality and safety of the organs, tissues, cells and processing batches. An effective traceability system and adverse event reporting must be in place that will respect the mutual anonymity of the donor and the recipient.

1.6.1 Role of the state

The primary role of the state is to establish a legal framework within which transplant services can operate, monitor and report and ensure that some mechanism is in place for regulating the various elements required for an effective transplant service, including traceability. The legal framework should include transplant law, the circumstances in which organs, tissues and cells can be retrieved, the consent or authorisation needed, death certification and the regulation of health service providers or other bodies involved in
transplant services. The designation of a non-commercial national or international body
responsible for the allocation and distribution of organs, and where necessary also for tissues
and cells, has been recommended. Member states should set up a system of authorisation and
inspection of procurement organisations and tissue establishments (see also Council of
Europe Recommendation No. R (94) 1 on human tissue banks).

1.6.2 Education and training

States should ensure that a system is in place to provide education and training for all
personnel involved in the various steps of the transplant process to maximise the skills that
are available.

1.6.3 Standard setting

Again, the state should ensure that a legal framework is in place so that appropriate standards
are set and adhered to.

1.6.4 Vigilance system

The state has a duty to ensure mechanisms are in place for the protection of donors and
recipients. This should ensure rapid investigation of any untoward incidents occurring in
relation to the transplantation services, so timely corrective and preventative actions can be
taken.

1.6.5 Organ allocation

An effective allocation system is essential. This system has to take into account the short
time that some organs can be maintained in good condition prior to transplantation, and the
necessity to ensure that the organ is assigned to the most suitable recipient, according to pre-
defined criteria. The rules for allocation are organ specific and they should be transparent
and duly justified, taking particular account of medical criteria. Every state should ensure
that there is a waiting list registration system for potential recipients, managed by and
a legally recognised allocation organisation. There should be a mechanism in place to ensure
that patients are not on more than one transplant waiting list for the same organs, tissue or
cells. Transplant allocation may be co-ordinated by regional, national or international
organisations (see Council of Europe Recommendation Rec(2001)5 on the management of organ transplant waiting lists and waiting times).

1.6.6 Time frame in organ, tissue and cell transplantation

The time between retrieval and transplantation can vary from hours to years depending on the nature of organs, tissues and cells retrieved. Safety and quality evaluation procedures will take those differences into account.

1.6.7 International co-operation

Where matched tissue typed organs are needed for sensitised patients it may be very difficult to find matches. For some renal patients or HPC bone marrow (BM) recipients, it is unlikely that they will find a match within their own country. In these cases co-operation between states is necessary and in some cases it may be necessary to identify suitable donors worldwide. International co-operation and organ exchange of organs, tissues and cells is necessary to increase the chances of providing material an organ for patients in life-threatening situations. For these reasons states should ensure that there is good co-operation between their allocation organisations and those set up in other countries.
Chapter 2 – Quality management: principles for ensuring the quality of organs, tissues and cells

2.1 Introduction

To maintain public and professional confidence in the safety and efficacy of organs, tissues and cells, careful attention must be paid to all aspects of the quality of the organs, tissues and cells:

*Careful attention must be paid to all aspects of the quality of the organs, tissues and cells in order to maintain public and professional confidence in their safety and efficacy.*

This chapter outlines the general principles of quality management systems and more detailed specifications are outlined in the relevant chapters.

2.2 General principles

The quality of the organs, tissues and cells depends on two distinct aspects:

- the requirements or standards for the organs, tissues and cells; these are outlined in the various chapters of this guide;

- the quality management systems which enable the organs, tissues and cells to meet these requirements.

2.3 Examples of quality management systems

Different *number of* quality systems can be applied *throughout the chain from donor identification up to allocation* in the preparation, use and quality assurance of organs, tissues and cells.

Good manufacturing practice (GMP) is concerned with both the principles of quality management and the requirements of provision. The principles of GMP are laid out in *The Rules Governing Medicinal Products in the European Union, Volume 4: Medicinal Products for...*

The International Organisation for Standardisation (ISO) has a broader scope and involves the management of quality throughout the organisation. The International Standard ISO 9000 family has been approved by CEN (Comité Européen de Normalisation) as a European Standard covering quality management systems in general. These should be used in conjunction with the above mentioned references, which include the principles of GMP.

The EN ISO 9000: 2000 has four main components:

- ISO 9000:2000: quality management system fundamentals and vocabulary;
- ISO 9001:2000: quality management system requirements;
- ISO 9004:2000: quality management system guidelines for performance improvement;

ISO standards distinguish between quality management systems and the requirements for the graft/product. They have been developed to assist organisations (e.g. health care establishments) of all types and sizes to implement and operate effective quality management systems.

ISO 9001:2000 on quality management system requirements is particularly relevant to the provision of organs, tissues and cells, and five distinct requirements are listed:

- quality management system;
- management responsibility;
- resource management;
- product and service realisation;
- measurement, analysis and improvement.

2.4 Terminology

Terminology in different quality systems tends to overlap, but the vocabulary used in this chapter is derived from the definitions used by the EN ISO 9000:2000 series and the EEC Rules and Guidance for Pharmaceutical Manufacturers and Distributors. Definitions are
given in Appendix 4.

### 2.5 Basic requirements

These are generally presented in the following format:

- quality management *and change control*;
- personnel and organisation;
- premises, equipment and materials;
- documentation;
- procurement, testing and organ, tissue and cell processing;
- quality control and proficiency testing;
- validation of all processes;
- complaints and component recall;
- investigation of errors and accidents;
- appropriate disposal mechanisms of organs, tissues and cells;
- self assessment and external audits.

### 2.6 Quality management

Quality is the responsibility of all *personnel* involved in the organ, tissue and cell transplantation process. A systematic approach to quality management should be implemented and maintained.

#### 2.6.1 Personnel and organisation

There must be sufficient suitably qualified personnel to carry out all the tasks. Their tasks and responsibilities must be clearly understood and documented. All personnel should have clear, documented and up-to-date job descriptions.

There should be an organisation chart showing the hierarchical structure of the organisation and clear delineation of lines of responsibilities.
a. Key personnel

Key personnel in all organisations involved in the transplantation process (from the initial
donor selection stage to the final delivery of organs, tissues and cells) should include a
responsible person (RP), and a medical specialist/advisor, who may or may not be the RP. In addition, the organisation should include an independent head of quality assurance (QA
Manager).

b. Training

Personnel should receive initial and continued training appropriate to the duties assigned to
them. Training programmes should be in place. The effectiveness of all training programmes
should be monitored by regular assessment of personnel competency. Training should be
documented and training records maintained. Personnel should also be trained in quality
principles relevant to their work.

Personnel should have relevant knowledge of microbiology and hygiene and should be
constantly aware that microbial contamination of themselves, donors, recipients, organs,
tissues, cells and premises should be avoided. Hygiene instructions must be present in each
department and these instructions should be understood and followed strictly by all
individuals.

2.6.2 Premises, equipment and materials

Premises and equipment must be designed, located, constructed, adapted and maintained to
suit the operations to be carried out. Their layout and design must aim to minimise the risk of
errors and permit operations to proceed in an orderly sequence, and should allow effective
cleaning and maintenance in order to avoid cross-contamination and accidents.

a. Premises

Donor selection should be performed on the premises, allowing for confidential personal
interviews. Premises for each step in the transplantation process should comply with
recognised existing regulations.

Storage areas should be of sufficient capacity to allow orderly storage of the various
categories of materials and components. There should be dedicated secure and monitored
areas for the storage of the different categories of organs, tissues and cells, with effective
segregation of quarantined and released products.

Storage conditions for organs, tissues, cells and materials should be controlled, monitored
and checked. Appropriate alarms should be present to indicate when storage temperatures
fall outside acceptable levels. Alarms should be regularly checked. Standard Operating
Procedures (SOPs) should define the actions to be taken in response to alarms.

b. Equipment
All equipment that might influence the quality or safety of the product should be designed,
validated and maintained to suit its intended purpose and should not present any hazard to
donors, recipients or operators. It should permit effective cleaning. Maintenance, monitoring,
cleaning and calibration should be documented and records kept.

c. Materials
Detailed specifications for the purchase of reagents and other materials that might influence
the quality or safety of the product are required. Only materials from qualified suppliers that
meet the documented requirements should be used. Manufacturers should provide a
certificate of compliance for every lot of materials.

Equipment and materials should conform to international standards and European and
national licensing arrangements where these exist.

Inventory records should be kept for traceability and to prevent use of materials after their
expiry date. Apparent deviations in the quality and performance of equipment and materials
should be investigated and documented promptly. The outcomes of these investigations should be reported in a timely manner to the competent authority responsible
to the manufacturer.

2.6.3 Contractual arrangements
When two or more facilities have entered into an arrangement, or if there are third party
arrangements relating to procurement, processing, storage or distribution functions, the
relationships and responsibilities of each should be documented and compliance should be
guaranteed by professional standards by all parties. Facilities should perform on-site audits of
contract laboratories to ensure their compliance both with professional standards and technical manuals and their own requirements.

2.6.4 Documentation and record keeping

Documentation ensures that work is standardised and that there is traceability in all steps in the transplantation process. Documentation must enable all steps and all data affecting the quality of the organs, tissues and cells to be checked and traced, from the donor to the recipient and vice-versa. Written documentation ensures that work is standardised and prevents errors that may result from oral communication. All documentation should be traceable. Where oral communication is necessary, audio recordings may be useful.

Donor documentation in general and donor deferral records in particular must be subject to the same controls.

Documentation should be version controlled and cover at least the following items:

- a quality manual;
- specifications (materials, labels, equipment, organs, tissues, cells, reagents);
- standard operating procedures (SOPs);
- identification of risks and a risk mitigation plan;
- other procedures (e.g. cleaning and maintenance);
- records on performance of operations (e.g. notes on donor selection, quality control);
- protocols (e.g. audits, complaints);
- training and competency records on personnel.

Documents should be approved by appropriate and authorised persons, and should not be handwritten except for those parts where data have to be entered. Any alterations made on a handwritten record should be dated and signed.

Documents relating to the selection of donors and the preparation and quality control of organs, tissues and cells should be retained according to national regulations, and international and national regulations on data protection have to be taken into consideration.
Data can also be stored in ‘non-written’ form, for instance on computer or microfilm. Users should only have access to those categories of data for which they are authorised.

Detailed specifications should be prepared for each type of graft. A processing record should also be kept and this document should be dated and signed by the personnel responsible for preparation and quality control. Any deviations from the standard documented procedures should be recorded and reviewed and corrective action should be undertaken.

Whenever applicable, records of equipment validation, calibration, maintenance and repairs (and subsequent revalidation) should be maintained.

A computerised record-keeping system ensures the authenticity, integrity and confidentiality of all records but retains the ability to generate true paper copies. The hardware and software of computers should be regularly checked to ensure reliability. Computer programs should be validated before use. Only authorised persons should make changes to computerised systems and any such changes should be validated before use. Facilities should have an alternative system that ensures continuous operation in the event that computerised data are not available.

2.6.5. The assessment and mitigation of risks

Risk Assessment

The procurement, manipulation and distribution of organs, tissues and cells should be subjected to a comprehensive risk assessment. Where appropriate, a “process flow” diagram listing all relevant steps, processes, reagents, tests and equipment might form the basis for the assessment exercise. Risk mitigation strategies should then be developed to protect the product, the patient, personnel and the process itself as well as other processes being undertaken in proximity.

Risks might for example derive from:

– donor selection and screening
– procurement procedures
– biological properties of procured organs, tissues and cells
– the use of “open processes”
– the selection and/or expansion of cells by extended culture
– the absence of standardised quality control tests
– the use of potentially infective materials
– the condition of the recipient.

Risk mitigation

Risks associated with the procurement, manipulation, distribution, and transplantation of organs, tissues and cells might be mitigated by, for example:
– the collection and manipulation of cells in closed systems
– validated disinfection systems
– segregation of processes by physical means or campaign
– development of assays to determine product safety and efficacy
– establishment of optimal dosing regimens
– avoidance of reagents with undesirable immunological or toxicological effects
– use of culture techniques to eliminate cells with undesirable characteristics.

2.6.65 Selection, procurement, testing and processing/handling

a. Donor selection

The final quality of organs, tissues and cells depends on many factors and starts with the selection of donors. Donors should be carefully selected (see Chapter 3) according to agreed principles and/or national regulations.

b. Organ, tissue and cell procurement

The procurement procedure should be carefully controlled. Systems should be in place to ensure traceability and provide a complete audit trail. Preventive measures should be in place to minimise any contamination. Defects that may adversely affect the quality of the organs, tissues and cells must be documented and dealt with by the RP.

c. Preparation/processing

Processing and preparation must be in accordance with clear and detailed instructions, and precise adherence to these instructions is required to obtain a defined quality. The biological nature of the starting material results in a great degree of variability in the final graft. Regular quality control is therefore of great importance.

Closed systems should be applied wherever possible. New processing procedures must be
validated before they are introduced and whenever they are altered.

During the whole process all containers should be clearly labelled. There should be instructions concerning the type and method of labelling. Harmonisation of labelling systems (e.g. ISBT 128) should be considered.

2.6.76 Quarantine and Release Storage, distribution and transportation

Final products that have not yet been made available for distribution must be kept in quarantine and should be distributed only when all the required quality controls and laboratory tests have been completed and laboratory results meet the established requirements.

2.6.87 Quality control and proficiency testing

Quality control and proficiency testing should be in place. Generally speaking, quality control refers to activities such as verification steps and testing which are used to ensure that materials and processes meet the required specifications.

Internal Quality Control in a laboratory includes the following of laboratory procedures by using control samples and all procedures to correct and prohibit deviations.

External Quality Assessment (sometimes also called proficiency testing) involves analysis of unknown samples and evaluation of the results by a third party.

Proficiency testing (or validation) of personnel involves testing personnel in the performance of their tasks.

2.6.98 Traceability

There must be a system in place that enables the path taken by each donation to be traced, from the donor to recipient/disposal and vice versa. This system must fully respect the confidentiality of both donor and recipient.

Each donor/component should be assigned a unique identifier that may serve also as a lot number to identify the material during all steps from collection to distribution and utilisation. This unique number should be used to link the donor to all tests, records, grafts and other
material, and for tracking purposes, to the recipient. Records should include identification, clinical and laboratory evaluation of the donor, verification of the conditions under which the material was procured, processed, tested, and stored, and should indicate its final destination. Records should indicate dates and the identities of staff involved in each significant step of the operation.

2.6.109  Complaints and recall

All complaints and other information that raise concern regarding the graft should be documented, carefully investigated, dealt with as quickly as possible. Effective written procedures must exist for recalling defective/suspect product. These written procedures must encompass any look-back procedures which may be necessary. The procedures should be communicated to the end user. A mechanism for appropriate review and assessment of actions taken to address complaints should be established.

2.6.110  Investigation and reporting of deviations, incidents, of errors and accidents, and adverse events reporting

Organisations involved in the transplantation process should document incidents and deviations from established procedures and specifications. Procedures should be in place to identify the problems to be corrected, and to inform the relevant authorities as appropriate.

Organisations involved in the transplantation process should document errors and accidents (i.e., unplanned deviations from established procedures or norms) in order to identify problems to be corrected.

Priority should be given to investigation and reporting of incidents with demonstrated or potential risk to cause serious adverse events.

2.6.124  Self assessment, internal audit and external audit

Auditing is an essential tool and should be conducted in an independent way by designated trained and competent persons from within the organisation, according to approved protocols.
External audits by independent bodies are necessary. Inspections are external audits carried out by designated approved/competent authorities.

All audits should be documented and recorded. Clear procedures need to be in place to ensure that appropriate suggested corrective actions are taken. These actions and their completion should be recorded. A blame culture should be avoided.
Chapter 3 – Selection of donors

3.1 General requirements

In order to maximise the benefits and minimise the risks of the transplant procedure, the suitability of an individual donor of organs, tissues or cells should be based upon quality and safety. Organs, tissues and cells should be retrieved and preserved within appropriate time intervals to preserve the necessary biological functions. The time interval should be compatible with the period it takes to perform all the relevant investigations to ensure the quality and safety of the retrieved materials. Therefore, all these activities should be undertaken according to SOPs within a quality assurance programme and should include an appropriate microbiological risk assessment.

Living and deceased donors are the source of organ, tissue and cell donations. Although there are some common aspects to these two types of donor, the criteria for selection may vary for living or deceased donors. Therefore, the selection procedure for cadaveric and living organ, tissue and cell donation will be described separately.

3.1.1 Archiving of donor samples

Samples of blood, tissue and any other relevant donor material should be stored for referral purposes and archived according to local regulations. The samples must be linked to the donor.

3.2 Deceased donors

Deceased people may be considered potential donors if presumed or informed consent meets the legal requirements of the country. They have expressed agreement to organ, tissue or cell donation during life, or if their families have given consent or not objected, depending on the law in different countries. (Resolution (78) 29 On Harmonisation Of Legislation Of Member States Relating To Removal, Grafting And Transplantation Of Human Substances)
Organs should not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law. The doctors with responsibility for the care of potential organ recipients, or who participate directly in removal of organs from a donor, or in subsequent transplantation procedures, should not be the same doctors certifying the death of the potential donor.

3.2.1 Definitions

Deceased donors fall into two categories, heart-beating, and non-heart-beating donors. Organs are mainly retrieved from heart-beating donors, whereas tissues are procured from heart-beating and non-heart-beating donors. In some countries, organ donation from non-heart-beating donors is also permitted.

a. Heart-beating donors

Certification of death with ongoing cardiac function should follow legal requirements. Most countries recognise this state as “brain death”, as defined in laws and codes of practice. Strict testing according to agreed protocols is required to establish brain death beyond doubt. Countries are strongly advised to review and, where necessary, enact laws to cover adequate definition of death with ongoing cardiac function.

b. Non-heart-beating donors (NHBDs)

Organ retrieval from NHBDs is restricted in some member states. In those countries that permit the procedure, the method of death certification and the manner of obtaining consent prior to the retrieval procedure need to be carefully defined. NHBDs are persons with complete and irreversible cessation of all cardio-respiratory function, with consequent death.

Death certification for donors who are only providing tissues should follow national regulations.

3.2.2 The active detection system for deceased donors

Detection of potential donors is the starting point for transplantation. This is probably the most difficult transplant activity to subject to standard protocols. The only way to ensure that potential donors are not missed is to have a means of identifying and monitoring individual potential donors within donor pools in relevant hospitals or geographical areas. Proactive
donor detection programmes should be instituted in every acute hospital using specifically trained professionals in compliance with agreed protocols and ethical rules.

a. Procurement co-ordination

One of the principal goals of procurement co-ordination is to assure continuous and efficient co-operation between the different teams involved in donation, retrieval, implantation, sharing of organs and tissue banking. The responsibilities for procurement co-ordination include:

- identification of potential donors, using all the available tools and scientific knowledge to expand the donor pool as much as possible;
- providing appropriate information for potential donors’ family members, including which organs, tissues and cells are to be retrieved and the purposes for which they are intended;
- informing families that organs, tissues or cells found to be unsuitable for clinical transplantation will be discarded or, if permission is granted, may be used for research or educational purposes;
- ensuring consent or authorisation for donation in accordance with national regulations and maintaining the relevant documentation;
- obtaining the donor’s medical and behavioural history from appropriate relatives or other individuals;
- co-ordinating and distributing procured organs and tissues to the appropriate recipients through established sharing organisations. Donor-recipient pairing should be closely examined particularly in cases of sub-optimal donors, in order to optimise the use of donors;
- co-ordinating the retrieval teams and organising the retrieval procedure;
- assuring the safety, quality and transparency of all the procedures performed;
- informing families that reconstruction of the appearance of the donor will be performed following retrieval;
- informing the doctors and nurses involved about the results of donation.
b. Detection and procurement network

(i) Detection centre
This refers to those hospitals that collaborate in identifying potential donors. These hospitals may or may not have the capacity to diagnose death with ongoing cardiac function or to correctly maintain the donor or to organise procurement. Depending on the national laws or organisational network potential donors may be transferred to the centres assigned for procurement.

(ii) Procurement centre
This refers to hospitals with the capacity to diagnose death, to maintain donors correctly and to organise organ and tissue procurement performed by local or visiting teams. Organs are sent to the assigned transplant centre where the transplants are undertaken with respect to allocation rules. Tissues are transferred to the tissue establishment.

3.2.3 Evaluation of the deceased potential donor

a. General evaluation
After a potential donor has been identified, the next priority is establishing their suitability. It is important to ensure that, as far as possible, any organs, tissues and cells retrieved from a donor are of acceptable quality and do not pose unacceptable risks for the recipients. Donor suitability criteria should be established according to accepted medical standards. Donor evaluation should include an interview with a family or other relevant source, a detailed review of the medical notes, assessment of the medical and behavioural history, full physical examination, post-mortem examination (autopsy) findings, if performed, and laboratory tests. Specific criteria for each organ or tissue will be discussed separately. This information should be obtained by a trained professional.

(i) Medical and behavioural history
Standardised questionnaires should be used to obtain the following information:

- age: while there may be no definitive cut-off level for individual donations, with increasing age the presence of co-morbidity is likely to make donation less acceptable;
• cause of death in order to identify infectious and neoplastic diseases. If no autopsy has been done, the cause of death of the donor, as ascertained from the medical notes, should be documented in the donor record. The estimated time of death or aortic cross-clamping should be noted;

• clinical history (pre-existing diseases, in particular malignant disease, multi-system auto-immune disease, infectious disease, neuro-degenerative or neuro-psychiatric disease or diseases of unknown aetiology);

• behavioural risk and previous medical treatment of the donor that could compromise the function of an organ or represent an increased risk for infectious disease;

• history of chemical and/or radiation exposure, previous and current medication including immunosuppression, travel history or overseas residency to evaluate the risk of tropical infections such as malaria and trypanosomiasis;

• recent history of any immunisation with live viable vaccines;

• history of blood transfusions or transplant procedures, body piercing or tattoos in the twelve months preceding death;

• risk of transmitting prion disease. This includes a definite diagnosis or high suspicion of any transmissible spongiform encephalopathy in the donor, a family history of Creutzfeldt-Jakob disease and whether the donor was the recipient of human pituitary derived hormones, or of dura mater, cornea or scleral transplants;

• other relevant family medical history.

(ii) Clinical evaluation of the deceased potential donor

Prior to the retrieval of organs, tissues or cells from a potential deceased donor a detailed medical examination should be performed and documented. It is the responsibility of the person performing the procurement to document any gross anatomical findings found during the retrieval procedure.

This can be a recent ante-mortem or post-mortem external examination of the donor, or a limited autopsy, to look for evidence of high-risk behaviour, unexplained jaundice, hepatomegaly or jaundice, hepatitis or other infection, neoplastic disease or trauma to the retrieval site.

The donor’s profile should be documented with respect to the medical and behavioural history, including signs of obvious medical intervention, scars, skin or mucosal lesions.
For organ donors, the clinical evaluation includes the haemodynamic status during resuscitation, in particular hypotensive episodes, duration of mechanical ventilation, days in the ICU, the need for mechanical cardiac resuscitation and the use of inotropic and vasoactive drugs.

Medical history, clinical, haemodynamic, biochemical and pharmacological parameters are all needed to assess the general suitability of the deceased person as an organ, tissue or cell donor.

*(iii) Laboratory tests*

For testing, blood samples taken before cessation of the circulation are always preferable to those obtained afterwards. A procedure should be in place to ensure identification and access to any stored sample.

Samples should be taken as soon as possible from the time of cessation of the circulation; preferably within 24 hours. To avoid haemolysis, the samples should be centrifuged as soon as possible after obtaining them.

If a deceased donor received ante-mortem transfusions with whole blood, blood components, colloids or crystalloids during the 48 hours preceding death, a pre-transfusion sample should be used for testing. If this is not available an algorithm incorporating the timing, nature and volume of the fluids infused, the donor’s own blood volume as well as any blood loss from intra-vascular space should be employed to assess any resultant plasma dilution. If a post-transfusion sample is processed, it is necessary to evaluate if the percentage of haemodilution can determine false-negative results according to the sensitivity of the method used.

Screening and confirmatory microbiological tests should be performed in nationally accredited laboratories using appropriately validated testing techniques. Microbiological and serological tests are performed to minimise the risk of transmission of infectious disease.

If samples for microbiological cultures are obtained at the time of retrieval, samples of each retrieved tissue should be taken prior to exposure of the tissue to antibiotic or antiseptic containing solution. The culture technique should allow for the growth of both aerobic and
anaerobic bacteria and fungi. The results should be documented in the donor record.

Blood culture, if procurement is performed on a deceased donor, may be useful in evaluating
the state of the cadaver and interpreting the cultures performed on the grafts themselves.

Minimum tests include:

- Anti-HIV-1/2 Antibody;
- HBsAg, anti-HBc Antibody;
- Anti-HCV Antibody.

Additional tests can be mandated according to national regulations and the type of
transplantation. **Nucleic acid testing (NAT) is encouraged where appropriate and available.**
In order to maximise donor availability and ensure an acceptable level of safety, a thorough
evaluation of donor positivity for HBV/HCV markers with appropriate algorithms for
matching donors and recipients is required.

Other tests may be required in specific situations, e.g. syphilis testing.

- donation for immunosuppressed patients:
  - Anti-CMV Antibody;
  - Anti-EBV Antibody;
  - Toxoplasma antibody.
- in donors living in or coming from high-prevalence areas:
  - Anti-HTLV I Antibody, malaria, etc.

The occurrence and/or prevalence of important transmissible diseases is available at the
WHO website.

Other tests depend upon the organs, tissues or cells to be transplanted. These may include
some non-microbiological tests:

- ABO blood group and Rh(D) group and human leukocyte antigen (HLA) typing;
- red and white **full** blood cell count.
Any relevant biochemical tests should be performed as indicators of the integrity and function of the graft (see specific criteria).

\(b\). General donor exclusion criteria

(i) Transmissible diseases

At present there are few absolute exclusion criteria for organ and tissue donation. However, according to national rules individual cases may need expert advice locally to evaluate the suitability of some donations, e.g. donors with specific infections, and in-situ malignancies. General exclusion criteria are as follows:

- HIV, disease, or seropositivity;
- active malignant neoplasia in any location, except some primary and non-metastatic tumours of the central nervous system, basal cell carcinoma of the skin, and in-situ carcinoma of the uterine cervix (see special criteria for corneas, 3.2.3.d.(iv) and Standardisation of organ donor screening to prevent transmission of neoplastic diseases, Council of Europe, 1997^);
- severe systemic infections which are untreated or of unknown origin;
- prion risk: donors treated with extracts derived from human pituitary glands (growth hormone, etc.), a family history of Creutzfeldt-Jakob disease or similar transmissible spongiform encephalopathy or donors who have received a human dura mater graft;
- viral hepatitis: depending on national rules, organs from donors with HBsAg may be used for HBsAg positive recipients and organs from HCV positive donors may be used for HCV positive recipients (HCV PCR positive). Furthermore, a donor who is HbsAg negative but Hbc antibody positive is acceptable as a donor if HBs antibody is shown to be present in his blood.

(ii) Behavioural risks

Behavioural risks for HIV, HCV, HBV, and other transmissible pathogens (see Appendix 3) should be evaluated according to the type of graft and urgency.

(iii) Additional examinations during organ retrieval

Systemic diseases with possible effects on the grafts to be transplanted (e.g. collagen

^ This document is currently being updated by the Council of Europe’s Committee of experts on transplantation.
disease, systemic vasculitis) may require additional examination. The final decision to use transplants also depends on macroscopic evaluation by the retrieving surgeon, and if necessary, an organ biopsy histology.

c. Organ-specific selection criteria

Acceptance criteria for organs are mainly based on acceptable donor organ function. The criteria may vary from team to team and may depend on recipient characteristics.

The specific acceptability criteria for different organs are discussed in the following sections.

(i) Renal-specific selection criteria

General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. No age limit (see 3.2.3.a.(ii)).

Clinical history. Consideration should be given to chronic hypertension, diabetes mellitus, albuminuria and kidney disease.

Renal function. Consideration should be given to urine output, current and previous serum creatinine levels, creatinine clearance, urea, proteinuria, urinary sediment, ultrasound of the kidneys and urinary tracts.

In case of chronically impaired kidney function, biopsies may be performed to determine the nature of the underlying disease. Advanced, irreversible, chronic renal failure is a contraindication for transplantation. Acute impairment in a donor’s renal function may not necessarily be a contraindication as it may be reversible.

Procurement and perfusion. Consideration should be given to the macroscopic appearance, colour after perfusion, individual evaluation of anatomical variants, and vascular atherosclerosis. Depending on local rules, limited warm ischaemia may be acceptable for kidney acceptance.

After procurement. Biopsy of organs is optional for assessment of older donors and donors with vascular pathology, history of hypertension, diabetes or brain haemorrhage of no known cause. Mild histological changes with minor glomerular sclerosis and interstitial
fibrosis may be acceptable.

(ii) Hepatic-specific selection criteria
General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. No age limit (see 3.2.3.a(ii)).

Clinical history. Consideration should be given to previous viral, alcoholic or fatty liver disease, previous hepato-biliary surgery, uncontrolled abdominal infections, intoxication affecting liver function and liver trauma.

Hepatic function. Consideration should be given to liver transaminases, serum bilirubin, alkaline phosphatase, LDH, albumin and coagulation tests. Evaluation of liver enzymes should take clinical history into account.

Hepatic morphology. Liver ultrasonography may be used to exclude obvious fatty liver degeneration, cirrhosis and fibrosis or any morphological abnormality.

Procurement and perfusion. It is important to evaluate the colour of the liver before and after correct perfusion. Obvious liver fibrosis and cirrhosis or steatosis may exclude transplantation. Peri-operative biopsy to evaluate the degree of fatty degeneration can be performed. The degree of acceptable fatty degeneration may depend on the general condition of the donor and the recipient and may vary with the urgency of the condition of the recipient and the experience of the transplant team.

(iii) Cardiac-specific selection criteria
General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. This depends on the local protocols and the recipient’s condition (see 3.2.3.a(i)).

Clinical history. Consideration should be given to previous cardiac diseases (valvular, ischaemic, etc.), hypertension, diabetes mellitus, smoking or alcohol history, arteriosclerosis, hyperlipidaemia, thoracic trauma, time spent in the intensive care unit (ICU), cardio-respiratory arrest and body surface area measurement.

Investigation for acute myocardial ischaemia. This should include enzymatic changes such
as Troponin, CPK and CPK-MB fraction which should take clinical history and evolution into account. The electrocardiogram (ECG) should be normal. Atypical repolarisation can be accepted under certain conditions.

Morphological examinations. Echocardiography should evaluate contractility and the ejection fraction and valvular anatomy and function. Chest X-ray and coronary angiography should be considered where appropriate.

Haemodynamics during resuscitation and donor maintenance. This should include evaluation of blood pressure, oxygen saturation, haemoglobin, hypotension, occurrence of cardiac arrest, use and dosage of inotropic and vasoactive drugs, and central venous pressure and invasive haemodynamic measurements where appropriate.

Procurement and perfusion. Consideration should be given to the macroscopic appearance, contractility and coronary palpation.

(iv) Pulmonary-specific selection criteria
General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. This depends on individual donor/recipient evaluation and individual teams (see 3.2.3.a.(i)).

Clinical history. Consideration should be given to a history of pulmonary disease or smoking, active pulmonary infection, aspiration, purulent secretions, thoracic trauma and previous thoracic surgery.

Lung function. This should be assessed in order to exclude organs with inadequate gas exchange and ventilation function.

Morphological examinations: Chest X-ray, and where appropriate bronchoscopy and thoracic computer tomography should be considered.

Procurement and perfusion. Consideration should be given to the colour of the lungs, presence of atelectasis, tumours and appropriate insufflation.
(v) Pancreatic-specific selection criteria

General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. This depends on the local protocols (see 3.2.3.a.(i)).

Clinical history. Consideration should be given to previous pancreatic disease, alcoholism, diabetes mellitus, active abdominal infection, abdominal trauma, number of days spent in the ICU, cardio-respiratory arrest, resuscitation manoeuvres.

Pancreatic function. This may be assessed by glucose and insulin requirements, pancreatic enzymes and calcium levels. Evaluation of pancreatic enzymes should take clinical history into account.

Morphological study. This can be assessed by pancreatic ultrasonography, magnetic resonance imaging (MRI) or other imagery.

Haemodynamics. Severe hypotension and cardiac/pulmonary arrest profoundly compromise the quality of the pancreas.

Procurement and perfusion. Consideration should be given to the macroscopic appearance, vascular and anatomical changes, and correct perfusion. The gross appearance of the pancreas should not have severe oedema or bleeding. Peri-pancreatic haematomas or capsular tears are a-risk factors for graft pancreatitis.

(vi) Intestinal-specific selection criteria

General selection criteria apply (see 3.2.3.a, 3.2.3.b).

There is no established guidance in the selection of these donors although the number of intestinal transplantations is still a recent innovation-increasing. Donors should preferably be CMV negative, but CMV positive donors may be used for CMV positive recipients if there is no CMV negative donor available.

The general donor selection criteria apply, depending on the local protocols.
Age. Depends upon the local protocols (see 3.2.3.a.(i)).

Clinical history. The criteria are similar to liver donation because most intestinal transplants are done at the same time as liver transplantation. Donors should not be obese. They should not have a history of alcoholism or uncontrolled abdominal infections, exposure to toxins affecting small bowel function, abdominal trauma, previous intestinal illness, diarrhoea, and they should have undergone less than five days’ hospital stay.

Gastrointestinal and liver evaluation. The following should be considered: serum electrolytes, liver function tests and liver enzymes. Evaluation of intestinal motility should be undertaken, which varies with length depending on duration of hospitalisation, haemodynamics during donor maintenance and the use of vasoactive drugs with vasoconstrictor effect.

Intestinal morphology. This can be assessed by abdominal ultrasonography to exclude ascites, other lesions and tumours. Abdominal X-ray or endoscopy may be used when appropriate.

Procurement and perfusion. Macroscopic view, intestinal peristalsis, vascular and anatomical changes and correct perfusion should be examined.

d. Tissue-specific selection criteria

General selection criteria apply (see 3.2.3.a, 3.2.3.b).

The general suitability criteria for organ donors apply. Suitability criteria need to be tailored to the intended use of the tissues. The following points also need consideration:

- age restrictions apply for some tissues;
- trauma or chronic pathology of the tissue;
- tumour or neoplasia of the tissue;
- microbiological infection of the tissue to be procured;
- specific warm ischaemia time before procurement may be relevant to some tissues;
- appropriate tissue function;
• poisoning with systemic toxic agents which are noxious for the particular tissue.

(i) Musculo-skeletal tissue specific selection criteria

Age. Cartilage, osteochondral allograft or meniscus donors should preferably be under 45 years of age. Donors of tendons or fascia lata (if for structural purposes) should preferably be less than 65 years of age. There are no maximum age criteria for femoral head donation by living surgical bone donors or if the cadaver bone is to be morselised, or if it is not for weight-bearing purposes (see 3.2.3.a.(i)).

Physical examination and clinical history. This is required to assess trauma or bone fracture. When large skeletal segments are obtained for structural support, the donor should preferably have had a low risk of osteoporosis. When metaphyseal and epiphyseal segments are obtained to provide structural support, closure of epiphyseal growth plates of the donor should be taken into account.

Donors with local irradiation, infection of the tissue or acute intoxication (cyanide, lead, mercury, gold) should be excluded.

Time limits for retrieval. Tissue should be retrieved as soon as possible after death. If the body has not been refrigerated, procurement of tissues should be completed within 12 hours of death. If the body has been refrigerated within 4 to 6 hours of death, procurement should preferably start within 24 hours and not later than 48 hours.

(ii) Cardiovascular tissue-specific selection criteria

Age. Donor age is usually up to 65 years. Each bank should determine its acceptable minimum age criteria for male and female donors, for premature infants and for different cardiac valves (see 3.2.3.a.(i)).

Specific requirements. History or evidence of endocarditis, myocarditis, rheumatic and other valvular heart disease may exclude donation, as may long-term corticosteroids treatment.

Chest trauma, particularly penetrating trauma (including intracardiac injection) should be evaluated.
History or evidence of open cardiac massage, cardiac infectious disease, valvular heart
disease and previous cardiac valve surgery may exclude donation.

*Time limits for retrieval.* As for musculo-skeletal tissue.

**(iii) Skin tissue-specific selection criteria**

*Age.* No age limit applies to skin donation (see 3.2.3.a.(i)). Acceptance criteria depend on an
individual’s size, skin condition and state of health.

*Specific requirements.* The external physical donor examination should detect cutaneous
lesions including dermatitis, fungal skin diseases, localised inflammatory skin disease or
abrasions and acute or non-healed burns, or macerated skin in the area to be procured. Acute
toxicity of skin containing known toxic chemicals, agents and poisons excludes donation.
Structural cutaneous disease such as collagen disease or auto-immune disorders should
exclude donation, as should previous radiation therapy or chemotherapy. Possible malignant
naevi should exclude donation.

*Time limits for retrieval.* As for musculoskeletal tissue.

**(iv) Ocular tissue-specific selection criteria**

This includes not only corneas, but also sclera and limbal stem cells.

*Age.* Age limits are determined by individual establishments (see 3.2.3.a.(i)).

*Specific requirements.* History of retinoblastoma or intraocular tumours, corneal dystrophy,
keratoconus, uveitis, corneal surgery including corneal laser surgery, ulcers, eye infections
or congenital or acquired disorders of the eye adversely affecting tissue to be transplanted
exclude donation. Donors with solid extra-ocular malignancies are generally accepted.

*Testing for HBe antibody for ocular tissue donors is not mandatory.*

*Time limits for retrieval.* The retrieval should be done as soon as possible after death. Eyelid
closure should be maintained. Eyelid closure, protective creams and cadaver refrigeration
may allow for prolongation of the time for retrieval. The time limit should be at the
discretion of the eye bank director. Retrieval later than 24 hours after death is acceptable, if
protective measures are ensured.

(v) Pancreatic islets-specific selection criteria
The criteria for pancreatic islets are similar to that of pancreatic acceptability. While
selection of donors for pancreas transplantation aims at reducing graft-related
complications, the selection of donors for islet transplantation is more of economical value
to avoid processing of organs with poor islet isolation outcome.

3.2.4 Donor documentation
Data concerning the organ and tissue donor procedure should be documented on
standardised forms. The following forms are recommended:

a. Donor information form
The donor information form should contain relevant information about the donor sufficient
to allow evaluation for eligibility for organ and tissue donation. The person referring the
donor to the referring hospital should complete the form. The form should accompany the
organs, tissues and cells and be maintained in the donor file. The form should be archived
separately from the recipient notes. In practice, for tissues, this information should be
maintained in the donor records in the tissue establishment.

b. Organ, and tissue, and cells report form
This form should contain data concerning donor organs, tissues, and cells at the time of
procurement. It should be completed by the procuring personnel and verified at the
end of procurement by the transplant co-ordinator. The time of aortic cross-clamping and
the start of cold perfusion, quality of perfusion, anatomical findings and time of organ
removal should be detailed. Separate forms should be filled out for each organ, and all
tissues, and cells to be transplanted.
c. Confidentiality
Donor and recipient confidentiality should be maintained.

3.2.5 Deceased organ and tissue donor management

a. Organ donor maintenance
Proper donor management should start as soon as possible after completion of death certification, and while appropriate consent is being obtained to maximise the chance of successful organ recovery.

Donor management is basically the responsibility of the doctor in charge of the ICU. It is recommended that a standardised protocol for donor management be developed in each centre, including monitoring and documentation. This should include:

- haemodynamic maintenance: monitoring and prevention of hypotension, hypertension, arrhythmias and cardiac arrest, and maintaining arterial pressure that guarantees correct organ perfusion;
- electrolyte maintenance: monitoring and correction of hypokalaemia, hyperkalaemia, hyponatraemia and hypernatraemia;
- temperature maintenance over 34 °C;
- endocrine maintenance: this should include the monitoring of clinical effects of and prevention of changes in the hypothalamic-pituitary-thyroid and hypothalamic-pituitary axis (diabetes insipidus) and changes in glucose metabolism;
- monitoring and correction of major coagulopathies;
- appropriate ventilation;
- renal function maintenance with prevention of polyuria and oliguria.

The incidence of irreversible cardiac arrest, sepsis and other contraindications to organ donation relating to the management of potential donors should be monitored and audited to identify problems and permit corrective action. The involvement of ICU staff in research and/or educational programmes on donor management should help raise standards.
b. Tissue donor maintenance

The time limits to retrieval and the temperature at which the cadaver should be maintained vary with the tissue to be retrieved (see tissue-specific selection criteria, 3.2.3.d). Every effort should be made to minimise microbial contamination.

3.3 Living donors

3.3.1 Definition

A living donor is a person who voluntarily donates an organ, tissue or cells to be transplanted. Organ removal from a living donor should only be carried out for the benefit of a recipient with whom the donor has an appropriate relationship as defined by law or otherwise with the approval of an appropriate independent body.

Donors of surgical residues are dealt with separately (see 3.4).

3.3.2 Pre-donation counselling of the potential living donor, informed consent and legal requirements

The donor should be given appropriate information as to the purpose and nature of the material to be removed, and the consequences and risks. The information should be supplied in advance and should be as accurate as possible, in terms the donor can understand. It should include the anonymity policy (anonymity obviously does not apply to related donation), any insurance arrangements and reimbursement of expenses. Significant abnormal findings should be reported to the potential donor with relevant advice. Where these findings do not result in donor deferral they should be reported to the transplant centre.

The donor should be made aware that the outcome of the transplant may not be successful despite his or her donation.

The principal risks for the donor are physical, arising from the surgical or other donation.
procedure. There are both short and long-term psychological and physical risks that need to be fully assessed. Before organ, tissue or cell removal, appropriate medical investigation should be undertaken to evaluate the donor’s health and the suitability of the material to be donated. This may include invasive procedures posing an additional risk for the potential living donor, for example, arteriography. The investigations should also include tests for viral and other disease, which might otherwise have been undetected and which could impair the health of the donor or be transmitted to the recipient.

According to national rules, informed written consent should be obtained from all living donors before such diagnostic procedures are performed. Informed written consent, or consent given before an official body, is also needed for the use of the donated material for specified purposes. Before signing consent the donor should have a face-to-face interview performed by an independent professional physician not involved with the transplant team, to avoid coercion (see Appendix 5: Additional Protocol). If the donor is a minor appropriate counselling should be given to the donor and parents/legal guardians. Fully informed consent must then be obtained.

Allogeneic haematopoietic precursor cell (HPC) donors must be made aware of the risk of death for the recipient if they withdraw after the conditioning therapy has started, the potential need for autologous blood transfusion at the time of bone marrow (BM) harvest and the use and potential side effects of cytokine administration for the mobilisation of peripheral blood progenitor cells (PBPC) (cytokine administration using G-CSF is only permitted in some countries). Some allogeneic donors may be asked to donate either HPC or lymphocytes for a second time and the donor should be made aware of this before the first donation.

In cord blood (CB) donation informed consent should be obtained from the biological mother and, in case of a surrogate mother, the woman carrying the baby. Consent for CB collection should be obtained prior to the collection procedure when CB is collected with the placenta in utero. The donor should be aware of the maintenance of long-term linkage for the purpose of notifying the donor/family of infectious or genetic diseases.
Potential donors may freely withdraw their consent at any time, except in the specific circumstances mentioned above. Protection of persons not able to consent to an intervention because of mental disability, such as adults who do not have the capacity to consent or for minors, should be secured in accordance with national law.

3.3.3 Evaluation of the potential donor

Health checks and in particular the psychosocial evaluation of all these types of donors should be undertaken by a physician uninvolved in the care of the potential recipient. The need for tissue typing of potential HPC donors should be undertaken at the discretion of determined by the transplant centre.

Donor evaluation test results should be fully documented by the donor selection centre and reported in writing to the transplant centre, to be evaluated by the physician undertaking the transplantation. Donor medical history, physical examination and testing should be completed and documented and the results available before any preparative or conditioning therapy of the recipient is begun. The use of a donor who does not meet all medical criteria requires careful consideration and documentation of the reason for his or her selection for donation according to the legislation in force. This will be done by the assessing physician in consultation with either the medical director of the donor registry (in case of an unrelated BM donor), and or the transplant physician as appropriate. For related donors this will be the responsibility of the assessment and transplant physicians and should be fully documented.

The minimal criteria for living donor evaluation are the same as in deceased donors. However, invasive pre-donation evaluation of the potential organ donor may also be necessary to ensure the suitability of the donor.

The psychosocial evaluation should include examination of the relationship between the potential donor and the recipient, and the reason for donation. The physician will rely on the information provided by the donor in a face-to-face interview, which will be documented in a standard questionnaire, and maintained in the donor records. The assessment should include:
• a comprehensive medical, behavioural and travel history with additional information obtained from the primary health care physician;

• a medical examination and tests to ascertain fitness to donate both with regard to the donor’s own health and suitability for the donation procedure, and to assess any risk of disease transmission to the recipient;

• where relevant, the donor size and blood group, tissue type and any other compatibility between donor and recipient;

• pregnancy: in living donors every effort should be made to avoid risk to the unborn child in pregnant women. This may lead to a temporary deferral.

3.3.4 Living organ donor selection

Living organ transplantation is rapidly growing. In some countries more than 50% of all kidney transplants performed are derived from living donors. Increasing numbers of hepatic segments derived from living donors are grafted and even pulmonary and intestinal segments have been transplanted.

Living donor procedures must only be performed in units with appropriate facilities and experienced teams. All living donors must be registered and offered lifelong follow up (Venice Conference on Safety and Quality in Organ Donation and Transplantation in the European Union, 17-18 September 2003).

General selection criteria and organ-specific selection criteria apply (see 3.2.3).

3.3.5 Haematopoietic progenitor cell (HPC) donor selection

a. Specific/Allogeneic/autologous BM/Peripheral Blood Progenitor Cells (PBPC) donors

General selection criteria apply (see 3.2.3.a, 3.2.3.b). In addition for allogeneic donors a family history of immunological, metabolic and haematological disease should be obtained to exclude any condition transmissible by blood.
Age. In accordance with *local/national guidelines* (see 3.2.3.a(ii)).

*Specific requirements.* For HPC donation a family history of immunological, metabolic and haematological disease should be obtained to exclude any condition transmissible by blood. A history of latex allergy should be elicited as well as a current or past history of back problems.

*Source of stem cells*

*In most autologous donors PBPC are the stem cell source of choice and are increasingly being used in the allogeneic setting. The choice between BM or PBPC in the allogeneic setting may be influenced by:*

- adequacy of venous access
- assessment of fitness to receive GCSF administration
- a current/past history of back problems
- fitness to undergo a general anaesthetic

*After donation.* Storage, manipulation, transfusion of these cells. *Any manipulation* should be performed as soon as possible after donation and *after collection and the cells should preferably be cryopreserved or transfused* within 24 hours.

*b. Specific Autologous BM or PBPC donors/patients*

General selection criteria apply (see 3.2.3.a, 3.2.3.b).

Age. In accordance with local guidelines (see 3.2.3.a(ii)).

*Specific requirements.* Autologous donors/patients should be fit enough to undergo the procedure and G-CSF administration where appropriate.

*After donation.* These cells should be cryopreserved as soon as possible after donation and preferably within 24 hours of collection.
Specific CB donor selection

This section will deal with allogeneic CB donation. Although the guidelines would also apply to autologous donors, the use of CB in an autologous setting is usually not generally recommended, and must be reserved only for specific, well-documented cases.

General donor selection criteria apply (see 3.2.3.a, 3.2.3.b). Any abnormal findings should be reported to the mother or with her permission to her or her child’s physician in writing.

Age/Gestation. CB units should be obtained from infants after at least 34 weeks of gestation (see 3.2.3.a.(i)).

Clinical history. A genetic history including ethnicity should be obtained and documented from the biological mother and from the father, if available. A family history of inherited disorders transmissible by HPC should be obtained. The history should detail any inherited disorders of the haematopoietic, metabolic or immune systems. In member states where a surrogate mother is allowed to carry a fertilised egg to delivery, an infectious disease risk history of the surrogate should also be obtained and documented. History of the current pregnancy and delivery, and the infant’s birth data should be obtained and documented, including gender, gestational age, other results of clinical examination and, if available, any disease diagnosed prior to discharge.

Laboratory testing. The maternal donor should be tested for the usual markers of infection no more than 3 days prior to delivery and up to 7 days after collection of the CB unit.

After donation. Storage of these cells should be performed as soon as possible after donation and preferably within 24 hours.

dec. Second donations

These are further donations of HPC or cells for CIT marrow, peripheral blood or leukocytes by a donor who has already given BM or PBPC HPC to the same patient. Individual assessment of each request is required to ensure there is a reasonable expectation of patient benefit. Before such donations the donor must be reassessed with appropriate testing and counselling, and consent should be obtained.
3.4 Collection of surgical residues

Surgical residues remain an important source of tissues and cells, and in some cases also organs (e.g. domino hearts and livers). They are collected during a surgical procedure where the material is removed for therapeutic purposes other than to obtain organs, tissues or cells. For such procurement of tissue there are no risks to the donor that are specifically related to the retrieval procedure.

The same conditions as for collection of surgical residues apply also for collection of foetal membranes (amnion and chorion) following delivery.

Informed consent should be obtained from the donor according to national rules. The minimum selection criteria are the same as for a deceased donor.

The anonymity policy should be respected at each stage of such collection of organs, tissues or cells.

3.5 Re-testing of living donors of stored allogeneic material

In living tissue/cord blood donors, re-testing for transmissible diseases after 6 months is mandatory unless the donated tissue underwent a terminal validated inactivation step. If re-testing is not performed, then tests of higher sensitivity (validated NAT antigen testing) may be performed from the initial sample in line with national guidelines.
Chapter 4 – Organ procurement and preservation

4.1 Deceased donors

Before the procurement begins, the identification of the deceased donor should be made by at least one member of the retrieval staff. Donor identity verification should be documented in the retrieval record, which should also include the source of the verification information.

Multi-organ donation should be encouraged. Teams from different transplant centres may retrieve specific organs. The timing of the retrieval teams has to be co-ordinated to minimise the risks of adversely affecting the viability of the organs and to limit disturbances for the donor hospital. The contacts within the donor hospital should preferably only be approached by the transplant co-ordinator(s) and not by different members of the retrieval team(s). After allocation of the extra-renal organs a timetable should be agreed upon, taking into account the needs of the donor hospital, travel time of the retrieval team(s) to the donor hospital and that of the organ recipient(s) to the transplant centre(s). Information about any delays should be appropriately communicated and acted upon. In case of unexpected anatomical findings additional examination, for example through biopsies, should be performed and the recipient team(s) informed about the final diagnosis.

The technique of the surgical team(s) should take into account the quality of organs and tissues to be removed and their appropriate handling after removal. In addition the team(s) should have responsibility for the physical reconstruction of the body’s appearance, which should be altered as little as possible. Procurement strategy should include agreement about responsibility for closure of the donor.

4.1.1 Facilities, staff and equipment for organ procurements

The donor hospital requires an operating theatre provided with the appropriate facilities and staff qualified in organ retrieval. Because the most common time for the donor to become unstable is during transportation from the ICU to the operating theatre, the anaesthetic team, with appropriate equipment at their disposal, should be involved before transportation of the
donor takes place. Environmental safety procedures should be followed according to general
hospital standards.

4.1.2 Multi-organ procurement procedure

a. Thoracic and abdominal organ procurement

Two separate teams usually perform multi-organ procurement, working separately on the
thoracic organs and abdominal organs. The procedure starts with a laparotomy and dissection
of the abdominal organs. Whenever stable donor conditions permit, appropriate time should
be given to accommodate in-situ splitting of the liver. However, the quality of the other
organs should never be compromised by such a procedure. In case of any deterioration in the
donor’s condition splitting of the liver may be continued on the back table of the operating
room. Then the thoracic team performs a sternotomy (if it was not performed initially) and
inspects and dissects the thoracic organs. Both teams commence in-situ perfusion of the
organs simultaneously after cross-clamping of the aorta. Topical cooling of the organs is
performed while awaiting the end of the perfusion. The thoracic organs are removed, then
the abdominal organs are removed. Preparation is continued on the back table if necessary.
After the organs to be transplanted have been removed, the abdominal surgeons can procure
large vessels and remove material for HLA typing and cross match testing between the donor
and the recipients (spleen, lymph nodes).

If non-heart-beating donor procedures are considered appropriate protocols should be in
place to avoid prolonged warm ischemia time.

b. Pancreas procurement for islet cell isolation

As the pancreas is very sensitive to warm ischaemia and as its retro-peritoneal localisation
makes local cooling difficult, the time between aortic cross-clamping and retrieval of the
pancreas should be kept as short as possible. However, as pancreatic islet cell transplantation
is not in itself a lifesaving procedure, priority should to be given to procurement of the heart,
lungs and liver. To avoid contamination of the kidneys, which may be retrieved after the
pancreas, the duodenum should be filled with a disinfection solution prior to its sectioning.
4.2 Living donation

Living organ donors are selected according to the criteria in Chapter 3. Generally, recipients of organs from a living donor should fulfil the same criteria for being placed on the same waiting list as for recipients of cadaveric organs.

4.2.1 Kidney donation

The decision on whether to perform a left or right donor nephrectomy should be based on the anatomical findings of the pre-donation evaluation. In no case should the donor be submitted to a higher peri-operative risk because of anatomical variations detected by the pre-donation screening. The choice of surgical access – whether open or laparoscopic – will depend on the donor’s preferences, the experience of the surgical team and the presence of general contraindications for a laparoscopic approach. As a general rule, the type of surgical approach should not compromise either the safety of the donor or the quality of the graft.

4.2.2 Liver donation

The size and line of resection will be determined by the anatomical findings of the pre-donation evaluation of the liver. The required volume of liver tissue to be resected from the donor for the recipient has to be determined using the best available methods of evaluation and has to ensure the safety of the donor.

4.2.3 Facilities and equipment for organ retrieval

The organ retrieval operation should be performed according to general surgical standards. The same medical care should normally be available for the donor and the recipient. The two operations (retrieval and transplantation) should be performed physically close to each other, to synchronise the two procedures and minimise the cold ischemia time.
### 4.3 Organ preservation, packaging, transportation and traceability

#### 4.3.1 Preservation

The removed organs should be flushed with cold preservation fluid. Donor blood should be removed as carefully as possible from the vessels of the organ, while keeping the organ cool in order to slow down its metabolism. Acceptable cold ischemia times should be specified for each type of organ and be kept to the minimum possible, as it is generally agreed that short preservation time correlates with better organ function.

The retrieval team should provide a sufficient amount of preservation solution. The solutions should be specified in SOPs and comply with existing national regulations. Possible contamination of the preservation fluid should be avoided and these fluids should be monitored with repeated samplings for bacterial culture. The required temperature should be achieved by external cooling, and continuous monitoring of temperature in the environment of the graft should be provided.

#### 4.3.2 Packaging/containers for organs

The retrieval team should provide all the necessary blood tubes, containers and transport coolers. The organ should be immersed in an appropriate solution and kept in two or three-fold sterile packaging. Packaging material should be inert, impermeable and sterile. All the packaging material should be validated for the intended use, including maintenance of temperature within the specified range for the specified time. The outer container should be thermally insulated and made of material robust enough to withstand leakage of contents, shocks, pressure changes and other possible conditions during transportation. The retrieved organs should be labelled with all the necessary details while preserving the anonymity of the donor. Labelling should include the following as a minimum:

- donor identification;
- place of donation;
- time and date of donation;
- time of start of perfusion;
• content of the package including the human origin and identification of the organ as right or left, *where appropriate*;
• address of destination.

Before release for transportation it is mandatory to check the contents of the package and ensure that all relevant information and documentation is provided, along with the appropriate labelling.

### 4.3.3 Information

The responsible transplant surgeons and transplant co-ordinators should be notified of the progress and results of all procedures pertinent to the organ retrieval operation. In case of delayed procurement time the recipient centre(s) should be informed. Detailed organ report forms should be available and kept for all procedures. All retrieved organs should be provided with an organ report form to include the following information:

• donor identification, while maintaining donor anonymity;
• relevant medical details;
• microbiological tests results;
• tests relevant to the viability of the organ;
• type and volume of preservation fluid;
• time of perfusion and explantation;
• morphological details of the explanted organ;
• identification of surgical team;
• donor hospital;
• institutions where organs are to be delivered.

### 4.3.4 Organ transportation

Transit time should be minimised. If transportation is within the same hospital the transportation should be designed to keep the organ in good condition and to protect the hospital staff. For transportation outside the hospital the shipping container should conform to local, national and international regulations. The receiving facility should verify that the
indicated storage temperature and proper condition of the shipped organ has been
maintained. It is the responsibility of the procurement co-ordination team to organise
appropriate transportation.

4.3.5 Traceability of organs

According to national rules it is the responsibility of the allocation organisations to ensure
that all transplanted material can be traced forward to recipients and back to the donor. It is
mandatory to inform the relevant contacts of donors or other recipients about potential
problems coming to light after transplantation, when relevant to their health. (see also 2.6.8
on traceability)

4.3.6 Feedback

After organ procurement completion, feedback notification and a letter of thanks should be
sent to the donor hospital.
Chapter 5 – Tissue and cell procurement

5.1 Procurement from deceased donors

Identification of the deceased donor by at least one member of the retrieval staff should be made before procurement begins (see also 5.3 and 5.4).

The ideal procurement facility should be an operating room, or another suitably validated location, depending on specific requirements for the tissue procured.

The following points should be considered for the tissue retrieval procedure:

- every effort should be made to minimise contamination during procurement;
- tissues may be removed using an aseptic technique. Clean, non-sterile techniques (see Appendix 4 for definitions) may be used if validated sterilisation/decontamination of tissues is employed. Where possible, sterile single-use instruments (disposable) should be used for tissue retrieval and also for processing. The general site of retrieval should be documented and area access should be restricted. All working surfaces used during retrieval should be disinfected;
- before retrieval begins the cadaver skin should be prepared using an appropriate antibacterial agent;
- every effort should be made to minimise the number of people present during retrieval. Retrieval should not be carried out if an autopsy is under way in the same room;
- if permitted by national law, it is preferable to carry out retrievals before the autopsy;
- a local sterile field using sterile drapes should always be used for procurement of tissues;
- all instruments used during the retrieval should be sterile and stored on a back table covered with a sterile drape;
- staff conducting the retrieval should be appropriately gowned and wear gloves and protective masks;
• aesthetic aspects and cadaveric reconstruction: skin should not be procured from the
  neck, arms, face or other areas that may affect funeral viewing. Following tissue
  procurement, the donor’s body should be reconstructed as closely as possible to its
  original anatomical configuration, to enable the usual funeral proceedings to take
  place;
• documentation of deceased donor reconstruction should be maintained in the donor’s
  record;
• every effort should be made to ensure that tissue retrieval is conveniently timed to fit
  in with funeral arrangements and other formalities.

5.2 Procurement from living donors

Tissues and cells should be collected under aseptic conditions during a surgical procedure
performed in the operating theatre or another suitably validated location, depending on
specific requirements for the tissues or cells procured.

5.3 Donor identification

Identification of the donor by at least one member of the retrieval staff should be made
before procurement begins. Donor identity verification should be documented in the retrieval
record, which should also include the source of the verification information.

5.4 Donor identification number

Each donor should be assigned a unique donor identification number to facilitate tracing of
the tissues. This unique donor identification number should be assigned either at the time of
procurement or on arrival at the procuring establishment.
5.5 Labelling and packaging

a. Procurement container

Each tissue or cell component should be packaged individually as soon as possible after retrieval using sterile, properly pre-labelled containers so as to prevent contamination between donations and ensure full traceability.

b. Procurement container integrity

After the filling and closing of the container, it should not be reopened nor the tissue removed until ready for use or further processing, by the procuring establishment.

c. Antibiotic immersion

If disinfectants or antibiotics are used after retrieval, samples for microbiological examination should be taken before the tissue is immersed in a disinfectant or antibiotic solution. Solutions used should be specified in SOPs and the antibiotic solutions should be validated for the purpose.

d. Temperature

Tissue should be maintained at environmental temperatures as defined in SOPs until the time of transportation to the processing centre. Maintenance of such temperatures should be documented.

e. Procurement container labelling

Containers should be properly labelled and with the donor and tissue or cell identification as containing human material, the name and address of the shipping facility and the intended receiving facility. Containers should comply with additional labelling requirements established by common carriers or by local, national, or international law.

The labelling should indicate:

- *name and address of the shipping facility and the intended receiving facility*;
- donor identification;
- place of donation, date and time of collection;
• content of the package, including the human origin and the identification of tissues and cells;
• for directed donation, a unique recipient identification.

5.6 Procurement documentation

Appropriate records for each donation procedure and for all the tissues or cells retrieved should include information pertaining to donor selection as in Chapter 3, and should be kept by the procuring establishment according to existing regulations. The retrieval documentation should include, but not be limited to the:

• name and address of the institution which performed the retrieval;
• date and time of the retrieval and the person responsible for the retrieval;
• place of the retrieval;
• donor name, age and gender (identification number if relevant);
• specific tissues retrieved;
• type, volume, lot, number and manufacturer of any additives, reagents and solutions used during the retrieval;
• signature of the responsible staff member;
• for directed living donations, the recipient’s identification.

5.7 Storage and transportation to processing facility

5.7.1 Temporary storage and transportation

The mode of temporary storage and transportation of procured tissue or cells to the establishment for processing depends on the tissue or cells concerned. Storage and transportation conditions should be specified in SOPs and should comply with local, national or international regulations.
5.7.2 Quality control of procurement and transportation

Quality control checks of procurement and transportation methods should be reviewed regularly to assure that integrity of tissues or cells and storage temperature are maintained during procurement and transit.

5.8 Haematopoietic Progenitor Cells (HPC): specific issues

5.8.1 Types of donation

HPCs can be obtained from a variety of sources that include bone marrow (BM), peripheral blood progenitor cells (PBPC) and cord blood (CB). These may be autologous or allogeneic, however, in general terms, these should all both meet the same quality standards.

5.8.2 General considerations for HPC BM and PBPC collection

Collection facilities should have access to a laboratory for progenitor cell assays, which should be accredited where national or international accreditation schemes are available. The laboratory should take part in external quality assessment schemes for CD34+ cell quantitation.

a. Bone marrow collection

BM harvesting is an aseptic process that should be undertaken in an operating theatre by an appropriately trained member of staff. A 24-hour blood component support including the provision of CMV antibody negative (or equivalent) and irradiated and leukocyte-depleted blood components should be available although blood transfusion in allogeneic donors should be avoided wherever possible. Whenever possible, it is recommended that autologous red blood cell donation be available for an allogeneic donor. Autologous red cell donation pre harvest may be considered but is not generally necessary. If autologous blood is taken it must be taken in a collection facility that meets applicable national/ international requirements. In Bone Marrow donation the maximum volume of donation, calculated for each individual donor, should be agreed nationally and in general should not exceed 15-20 mls/kg donor weight.
b. Peripheral blood progenitor cell (PBPC) collection

PBPC should be collected in a facility where staff have appropriate experience in both
aphaeresis and PBPC mobilisation. There must be resuscitation facilities on site. Wherever
possible, peripheral veins should be used for venous access and in all circumstances due
consideration should be given to the safety of the donor in the placement of central venous
catheters.

c. Cord blood collection

It is important that procedures and practices in CB collection protect the mother and infant
and that no modifications in delivery practices are made to increase CB volume. Each CB
facility should have an appropriately qualified responsible person who should ensure that
off-site collections meet agreed national/international guidelines.

5.8.3 Dose requirements

The transplant physician should specify in writing Processing and transplant facilities
should agree on the dose (nucleated cell count, mononuclear cell count, CD 34 positive cell
count and/or clonogenic assays as appropriate for the source of HPC) required to achieve
reliable and sustainable engraftment. In CB the volume of the collection correlates to the
dose and must also be accurately measured. Each facility must agree on a minimum
acceptable volume for processing. In BM donation the maximum volume of donation,
calculated for each individual donor, should be agreed on nationally.

5.8.4 Additional testing

Any assays performed on HPC (e.g. nucleated cells, mononuclear cells, CD 34 positive cells
and/or clonogenic assays) should be performed in an nationally accredited laboratory which
participates in appropriate external quality assessment schemes.
Chapter 6 – Tissue establishments

6.1 General organisational requirements of a tissue establishment (TE)

6.1.1 Institutional identity

a. General

The purpose of the tissue establishment (TE) should be clearly defined and documented, as should its organisational, reporting, and accountability structure. The establishment should ensure that all staff are professionally competent for their tasks and offer appropriate training as necessary.

b. Licensing

The TE should comply with all relevant national or European laws or regulations for accreditation, authorisation, registration or licensing.

c. Information technology (IT)

Appropriate IT systems should be used.

6.1.2 Organisation

a. Responsible person

(i) General

Tissue establishments should designate a responsible person to supervise the procedures and policies of the establishment. This person should be qualified by training and should possess a diploma, certificate or other evidence of formal qualifications in the field of medical or biological sciences awarded on completion of a university course of study or a course recognised as equivalent by the member state concerned. He/she should have at least two years of practical and relevant experience for the scope of activities being pursued.
(ii) Responsibilities

The person referred to above should be responsible for determining what tissues are to be collected, defining donor screening policies and prescribing technically acceptable means for their processing, quality assurance, storage and distribution. The designated person should be responsible for policies and procedures regarding donor suitability and adverse reactions. The responsibilities for medical issues should be delegated to an appropriate medical specialist.

The responsible person should ensure that human tissues and cells intended for human application in the establishment are procured, tested, processed, stored and distributed according to this guide and the laws in force in member states.

The responsible person should assure, that the tissue establishment must have has a quality management system in place (see Chapter 2).

b. Procedures manual

The establishment should maintain an SOP manual covering all aspects of donor screening, retrieval, processing, testing, storage and distribution practices. The SOPs should be used to ensure that all material released for transplantation meets at least the minimum requirements defined by professional standards and applicable European, national, state, and local regulations. The SOP manuals should include where relevant, but should not be limited to, the following:

- standard procedures for donor screening, consent, retrieval, processing, preservation, testing, storage and distribution;
- quality assurance and quality control policies;
- laboratory procedures for tests performed in-house and in contracted laboratories;
- specifications for materials used including supply, reagents, storage media and packaging materials;
- personnel and facility safety procedures;
- standard procedures for facility maintenance, cleaning and waste disposal procedures;
- methods for verification of the effectiveness of sterilisation procedures;
• equipment maintenance, calibration and validation procedures;
• environmental and microbiological conditions and the methods used for controlling, testing and verification;
• physiological and physical test specifications for materials;
• methods for determination of shelf life, storage temperature and assigning expiry dates of tissues and cells;
• determination of insert and or label text;
• policies and procedures for exceptional release of material;
• procedures for adverse reactions reporting and corrective actions;
• donor/recipient tracking and product recall policies and procedures.

All SOPs and associated process validation studies should be reviewed and approved by the responsible person. Copies of the procedure manual should be available to all staff, and to authorised individuals for inspection upon request. Upon implementation, all SOPs should be followed as written. SOPs should be updated at regular intervals to reflect modifications or changes. The date of the change coming into effect should be noted along with the reason for the modification if it is not obvious. Possible shortcomings of the previous procedure should be mentioned if they have become apparent. The responsible person should approve each modification. Appropriate training should be provided to the staff concerned. Obsolete procedural manuals should be archived for a minimum of 10 years, taking into account the shelf life of the material.

c. Records

(i) General

Records should be confidential, accurate, complete, legible and indelible. All donor, processing, storage and distribution records should be maintained for 30 years after clinical use, or expiry date of the tissues and cells (whichever occurs first), or in accordance with European, national or local law.

Detailed records should be made concurrently with the performance of each step in the donor screening, collection, preparation, testing, storage and distribution of material in such a manner that all steps can be clearly traced.
(ii) **Inventory**
A record of unprocessed, processed, quarantined and distributed tissues should be maintained.

(iii) **Recipient adverse events and non-compliances**
An adverse reactions file should be maintained (see 6.10 and 7.4.3) including any non-compliances. Serious adverse reactions should be reported to the competent authorities.

d. **Ethics committee requirements**
Establishments should have access to relevant research protocols for all banking activities and appropriate donor consent forms. As required by local and national governmental regulations, the establishment should maintain documentation of all protocols, ethical committee approvals, new drug or device exemptions and any adverse outcome reports.

### 6.2 Facilities and equipment

#### 6.2.1 Facilities and equipment in a tissue establishment

*a. General*
The facilities of the establishment should be of suitable size and location, and should be designed and equipped for the specialised purposes for which they are to be used.

Where tissues or cells are processed in open containers facilities should have:

- floors, walls and ceilings of non-porous smooth surfaces that are easily sanitised;
- temperature control;
- for sterile processing, air filtered through high-efficiency particulate air (HEPA) filters with an appropriate pressure differential between zones that can be documented;
- a documented system for monitoring temperature, air supply conditions, particle numbers and bacterial colony forming units (environmental monitoring);
- a documented system for cleaning and disinfecting rooms and equipment;
• a documented system for gowning and laundry;
• adequate space for staff and storage of sterile garments;
• access limited to authorised personnel.

b. Design
Laboratories should be designed to prevent errors and cross-contamination. Critical procedures should be performed in designated areas of adequate size.

c. Security
Access to restricted areas of the establishments should be limited to authorised persons.

d. Environmental monitoring
Environmental monitoring procedures should be established, when appropriate, as part of the quality assurance programme. The procedures should include acceptable test parameters. The monitoring may include particulate air sampling and work surface culture. Each monitoring activity should be documented.

e. Sanitation
Facilities used for retrieval, processing or preservation, where there is potential for cross-contamination of material or exposure to blood-borne pathogens, should be subjected to routine, scheduled and documented cleaning and disinfection procedures.

f. Equipment
Equipment and instruments should be of a quality appropriate to their intended functions. Equipment and non-disposable supplies that come into contact with tissue or cells should be constructed so surfaces do not alter the safety or quality of the biological material. Equipment should be designed, manufactured and qualified for appropriate cleaning and should be sterilised or decontaminated after each use. A separate set of clean, sterile instruments (disposable, where appropriate) should be used for each donor. There should be SOPs for monitoring, inspection, maintenance, calibration and cleaning procedures for all equipment. Refrigerators, freezers and other equipment required to maintain a specific temperature should be inspected on a regularly scheduled basis. Appropriate certification and maintenance records should be maintained for instruments and equipment.
6.2.2 Environmental safety of tissue establishments

a. General
Each tissue establishment should provide and promote a safe work environment by developing, implementing and enforcing safety procedures. Safety precautions and procedures for maintaining a safe work environment should be included in the SOP manual and should conform to European, national and local requirements.

b. Safety procedures
Safety procedures should include, but not be limited to, the following:

- instructions for fire prevention and evacuation routes in case of fire or natural disaster;
- procedures for prevention of worker injury including possible exposure to biohazards and to other hazardous material, such as liquid nitrogen;
- procedures for proper storage, handling and utilisation of hazardous materials, reagents and supplies;
- procedures outlining the steps to be followed in cleaning biohazard spills;
- hazardous material training, including chemical, biological and radioactive hazards;
- immunisation: appropriate vaccinations should be offered to all non-immune personnel whose job-related responsibilities involve potential exposure to blood-borne pathogens. Personnel files should include documentation of receipt of vaccinations or refusal of vaccinations;
- personnel: personnel engaged in the retrieval, processing, preservation and packaging of tissues and some cells should be suitably attired to minimise the spread of transmissible pathogens among and between donors, tissue and staff. Any staff member with a serious infectious condition should be excluded from tissue banking activities until the condition is resolved;
- accidents causing possibly an infection or serious injury to staff members have to be recorded. All preventive measures possible must be taken in accordance with local rules.
c. Waste disposal

Human tissue, cells and other hazardous waste items should be disposed of in such a manner as to minimise the hazards to the tissue establishment’s personnel or the environment, and should be in conformity with applicable European, national and local regulations. Proper disposal procedures should be applied to human remains.

6.3 Tissue and cell processing, preservation and storage

6.3.1 General

Tissues and cells should be processed and preserved appropriately for clinical use. Processing, preservation and storage steps should be validated.

6.3.2 Reagents and preservation solutions

The reagents used in preservation and processing should be of an appropriate grade for their intended use and be sterile, if applicable, and comply with existing national regulations. Possible contamination of preservation fluid should be avoided and monitored by repeated testing for bacteria and fungi. Whenever possible, reagents used for collection, processing and preservation should be approved for human use. Reagents not approved for human use may be used if reagents or procedures that include the reagent have been approved by national authorities or have been established in medical literature to be acceptable for the purpose specified. The origin, characteristic (physical, chemical, microbiological) conditions for storage and expiry dates of reagents should be monitored and recorded. Reagents should be used in a manner consistent with instructions provided by the manufacturer.

6.3.3 Pooling

Pooling is generally not recommended and can only be accepted for specific tissues. The size of the pool should be limited to the minimum number of donors and traceability to each individual donor must be ensured.
6.3.4 Quality control

Tests and procedures should be performed to measure, assay or monitor processing, preservation and storage methods, equipment and reagents to ensure compliance with established tolerance limits. Results of all such tests or procedures should become part of the permanent record.

6.3.5 Processing and processing environment

Processing should not change the physical properties of the material so as to make it unacceptable for clinical use. Facilities for aseptic and clean non-sterile processing should comply with The Rules Governing Medicinal Products in the European Union, Volume 4: Medicinal Products for Human and Veterinary use – Good Manufacturing Practice (2004), where appropriate. They should provide separate work areas with defined physical and microbiological parameters. Wherever appropriate, a validated pathogen inactivation/reduction or terminal sterilisation should be included in the process. Where tissues or cells are processed in open containers facilities should have:

- floors, walls and ceilings of non-porous smooth surfaces that are easily sanitised;
- temperature control;
- for sterile processing, air filtered through high-efficiency particulate air (HEPA) filters with an appropriate pressure differential between zones that can be documented;
- a documented system for monitoring temperature, air supply conditions, particle numbers and bacterial colony forming units (environmental monitoring);
- a documented system for cleaning and disinfecting rooms and equipment;
- a documented system for gowning and laundry;
- adequate space for staff and storage of sterile garments;

access limited to authorised personnel

The processing environment should comply with the recommendations for good manufacturing practice (GMP) and good laboratory practice (GLP).
6.3.6 Novel Processes Processing environment

The risks associated with the introduction of new processes (e.g. manipulation of immune cells for therapy) may not be fully characterised. Quality systems should include a carefully considered plan to control and manage these risks (see section 2.4.6). The processing environment should comply with the recommendations for good manufacturing practice (GMP) and good laboratory practice (GLP).

6.3.7 Preservation and storage

a. General

Tissues and cells should be processed and stored according to currently accepted practice, based on the best available scientific evidence, and according to GMP and GLP as appropriate for tissues and cells. The methods should be specified in SOPs. Currently accepted methods of tissue and cell preservation include:

- tissue and cell culture;
- hypothermic storage (refrigeration) above 0 °C but below +10 °C;
- freezing at –40 °C or below, with or without the use of cryoprotectants;
- freeze-drying;
- other dehydration methods.

b. Expiry date

A maximum recommended storage period with an expiry date should be assigned to all tissues and cells.

6.3.8 Reference samples for cord blood

The CB product reference samples should be stored deep-frozen in such a way that all necessary tests can be done.
6.3.8.9 Labelling

a. General requirements
There shall be written procedures designed and followed to ensure that correct labels, labelling, and packaging materials are used. Each labelling phase for all tissue or cells should be documented. Material should be labelled for identification and tracing during all phases of procurement, processing, preservation and distribution. Use of a unique donor identification number should be incorporated into the tissue identification label to facilitate donor-recipient tracking. Labelling should be clear, legible and indelible. In CB banking this also applies to any maternal specimens, the reference samples and their associated documents. For autologous or directed donations, the name and/or identifier of the intended recipient, if known, should be included.

b. Nomenclature
Standard nomenclature and SI units of measurement should be used to describe tissues and the processing they have undergone. Containers will be labelled so as to identify the tissue/cell product name and identification number.

c. Label list
A master label list of all labels that are used should be maintained as well as an example of every label that is utilised by the bank. Written procedures shall be designed and followed to ensure that correct labels, labelling, and packaging materials are used. Each labelling phase for all tissue or cells should be documented. Dates of use should be recorded.

d. Labelling integrity
Labels should be designed to adhere firmly to the container under all anticipated storage and transport conditions. The label applied by the bank facility should not be removed, altered or obscured.

e. Visual inspection
Prior to labelling a unit of processed material, the container should be inspected for evidence of impurities, defects, broken seals or contamination that could compromise the quality,
integrity or safety of the tissue or cells. A sufficient area of the container should remain uncovered to permit inspection of the contents whenever possible.

\[f. \textit{Container labelling}\]

Containers should be labelled with the following information in accordance with national regulations:

- description of the contents;
- full name of the tissue establishment;
- batch/lot/serial number;
- expiry date (for finished tissues that have a determined shelf life);
- special instructions for storage and handling conditions.

The following additional information can be provided on the container, if possible:

- tissue/cell identification number;
- date and time of procurement;
- disinfection or sterilisation procedure used, if applicable;
- preservative used and its concentration, or, if no preservative has been used, and the absence of a preservative is a safety factor, the words “no preservative”;
- amount of material in the container;
- potential residuals of added processing agents/solutions;
- results of screening tests performed and labelled with the warning “This product may transmit infectious agents”;
- directed tissues/cells intended for autologous use should be prominently labelled “For autologous use only” and the donor/recipient’s name identification provided;
- each cell unit intended for directed allogeneic use should be prominently labelled “For use by intended recipient only” and the recipient’s identification provided;
- the statement “See package insert”.

75
6.3.9.10 Package insert

Tissue and cells deemed suitable for transplantation should be accompanied by a summary of records documenting the fact that all required disease screening and testing has been completed, specifying that the results have been reviewed and accepted by the person responsible.

A package insert containing instructions for proper storage and thawing, where appropriate, should accompany all tissue and cells, covering graft preparation, handling and reconstitution where appropriate. Specific instructions should be enclosed for material requiring special handling.

6.3.11 Package insert requirements

Inserts should contain the following information if applicable:

- a statement limiting use to specific health professionals;
- a statement that the material is intended for use in one patient on a single occasion only;
- indications and contraindications for use of tissue and cells;
- appropriate warnings and a list of possible significant adverse reactions;
- instructions for opening the package and/or container, and for reconstitution;
- the expiry time (if applicable) of tissue or cells following reconstitution;
- instructions for preparation of tissues or cells for transplantation;
- a statement that the material was prepared from a donor who was nonreactive or acceptable when tested for the mandated microbiological tests, verifying that appropriate and licensed tests were used;
- a statement for non-sterilised material: “This tissue may transmit infectious agents”;
- a statement, if applicable, that the tissue or cells may not be sterilised or re-sterilised;
- recommended storage conditions;
- a statement that it is the responsibility of the end user to maintain the tissue or cells in appropriate storage conditions prior to transplantation;
- special instructions for each particular tissue, for example, “do not freeze”;
• the presence of known sensitising substances;
• the type and calculated amount of antibiotics and preservatives added during processing;
• a statement that adverse reactions potentially attributable to the tissue or cells should be reported promptly to the tissue establishment;
• a statement that it is the responsibility of the recipient hospital, or other material storage and distribution facility, or clinician, to maintain recipient records for tissue tracking post-transplantation.

6.3.10.12 Packaging

a. General
Packaging of the tissue or cells should be performed in a certified and qualified environment that should be specified in SOPs. Processing facilities should establish and document validated packaging protocols.

Packaging should ensure integrity and maintain sterility of the contents of the final container. Storage containers should be appropriate for the type of tissue or cells, type of preservation and its intended application. The container should maintain its integrity, withstand sterilisation and storage conditions, not produce toxic residues during storage and maintain tissue integrity and quality.

b. Visual examination
Each tissue or cell unit container should be examined visually for damage or evidence of contamination before packing processing. Packaged and labelled tissue or cells should be examined visually for appropriate labels, contents, container damage or broken seals and evidence of contamination prior to its dispatch.

6.3.113 Quarantining and quarantine areas

Human tissue or cells should be quarantined until the tissue or cells are determined to be suitable for transplantation. All tissue or cells should be quarantined until donor screening tests have been completed and reviewed by the person responsible and found to be
acceptable. Materials known to be or suspected of being infected should preferably be stored in separate refrigerators or freezers, or in liquid nitrogen containers.

3.124 Quarantine areas

Quarantine areas should be clearly labelled and physically separated from areas where tissue or cells available for distribution are stored.

6.4 Release of tissues or cells

Donor files and tissue or cell processing records should be reviewed to ensure that material is suitable for transplantation and implantation. Prior to the release of tissue or cells into the inventory for distribution, there should be documentation of: This will include:

- approval of donor eligibility by the responsible or designated person;
- review and approval of processing, preservation and storage records by the responsible or designated person;
- final inspection of both the label and container to ensure accuracy and integrity;
- screening results (e.g. microbiology/processing cultures) and other test results used to determine final release. These should be kept by the bank distributing the tissue or cells;
- exceptional release approved by the responsible person and transplanting physician.

Prior to the release of tissue or cells into the inventory for distribution, the responsible person or his designee has to document that all release criteria are met. If not all criteria were met yet, exceptional release may be approved by responsible person (see 6.9).

6.5 Distribution

Packaged and labelled tissue or cells should be examined visually for appropriate labels, contents, container damage or broken seals and evidence of contamination prior to its dispatch. Tissue or cell distribution for transplantation should be restricted to hospitals, banks, physicians, dentists or other qualified medical professionals and comply with national
regulations. There should be written SOPs and documentation for all tissues distributed. The
SOPs will describe final verification of release, distribution, procedures, documentation and
the collection of tracking information for all organs, tissues and cells distributed.

6.6 Traceability

Records should be maintained which document the origin and destination of distributed
material. The receiver of tissues or cells is responsible for verification of shipment and for
obtaining and retaining all recipient information. The receiver should provide prompt
information to the issuing centre about adverse reactions or technical problems with the use
of the allograft or autograft.

6.7 Transportation

Maintenance of defined (upper and/or lower parameters) environmental conditions during
transit as defined by the SOPs or institutional limits should be required. Transportation
arrangements should be appropriate and should not risk the integrity of tissue or cells. The
use of hazardous elements such as solid carbon dioxide or liquid nitrogen should comply
with respective European, national or local regulations.

6.8 Return into inventory

The establishment should have a policy authorising or prohibiting the return of material in its
original, unopened container to the establishment bank. The establishment bank should
ensure tissue or cell acceptability for transportation, including documentation of user storage
and shipping conditions. If there is any evidence of contamination, tampering, mishandling
or failure to maintain required storage and/or transportation temperatures, material should
not be returned to the inventory.

6.9 Exceptional release

If tissue or cells are distributed or dispensed for transplantation in an emergency situation or
under special medical conditions and in conformity with national regulations, provision for
an exceptional release and appropriate documentation should be established. Exceptional release follows a clinical judgement based on knowledge of the appropriate medical practice under particular medical conditions. Exceptional release will occur only with the authorisation of the responsible or designated person and does not preclude follow-up testing, donor screening and other quality assurance measures described in the SOPs. Distribution of tissues or cells through exceptional release will include a notice of exceptional release describing the nature and seriousness of the risk. Documentation of the exceptional release should be maintained in the donor record.

6.10 Recipient adverse events and non-conformances

All reported or suspected adverse events should be investigated thoroughly and expeditiously and reviewed by the responsible person medical director. Appropriate corrective and preventative action must be taken and documented. The receiver should provide prompt information to the issuing centre about adverse reactions or technical problems with the use of the allograft or autograft.

6.10.1 Notification

In accordance with European, national and local regulations, all serious adverse events such as identified transmission of disease should be reported to the public health authorities, processing institutions, and where relevant, to the donor’s personal physician (with the donor’s consent), and, to physicians involved in transplantation or implantation of the organ/tissue/cell.

When donor-to-recipient disease transmission through tissue or cell use is discovered all facilities involved in the procurement and distribution of organs and/or tissue from the infected donor should be notified in a timely manner. Notifications should be documented in both the donor and the recipient(s) records.
6.10.2 Recall

A written procedure should exist for recall of tissues. The establishment’s responsible person should ensure that all procedures are in place for recall or notification of possible contamination, defects in processing, preparation, distribution and other factors affecting suitability of organs, tissues or cells for clinical transplantation.

6.11 Hospital tissue and cell storage and distribution

a. General

Hospitals are responsible for establishing appropriate record-keeping and storage procedures to ensure the traceability of tissue, cells and recipients, and the maintenance of the safety and efficacy of tissues or cells from receipt from the establishment bank to clinical use. These standards should be made available to hospitals which receive material for transplantation and then issue it for transplantation or implants within their institution.

b. Storage

(i) General

Storage of materials for transplantation should conform to guidelines established by the distributing establishment and national regulations.

(ii) Records

Records should document the date and condition of tissue or cells on receipt and be maintained according to European, national or regional laws, regulations or guidelines.

(iii) Release and distribution

The release of material from storage should include a record of the establishment, transplant date, recipient’s name, unique identifier number and type of material, and the transplant surgeon. This information should be maintained in the hospital’s tissue and cell storage and distribution service and in the recipient’s medical records.
(iv) Adverse events and non-compliances

Reports of any adverse events including transmitted disease or other complications or non-compliances should be evaluated by the hospital and reported to the tissue or cell establishment. The reporting of these events should follow national health or regional health department guidelines.

c. Disposal of waste/surplus

(i) Tissue or cell discard

There should be a documented hospital policy for the disposal of material, unused or unsuitable for clinical use. Records should include details of the date and method of disposal and the reason for disposal. Material for disposal should be appropriately handled and disposed of in conformity with local guidelines.

The method of disposal and decontamination should meet European, national or regional laws, regulations and guidelines.

(ii) Disposal of directed-related haematopoietic stem cells

Disposal of haematopoietic progenitor cells (HPCs) should be in accordance with the agreement that was signed before collection by the facility contracted for storage and in agreement with the informed consent from the patient/donor at the time of donation.

There should be written documentation either of the patient’s death or of no further need for the component before any component is discarded, and disposal should follow existing regulations.
Chapter 7 – Transplantation practices

7.1 Organisational issues

Before starting any transplant programme, an appropriate organisational framework should be established. Personnel should be adequately trained in the field of transplantation. Implantation procedures should be carried out according to national rules by an authorised hospital transplant service. It is recommended that the results of transplant procedures be reported on a regular basis to relevant organisations to allow periodic evaluation of the effectiveness of corresponding transplant centres and of the procedures undertaken.

Written standard operating procedures (SOPs) should exist for detailed pre-operative evaluation and management, the transplant procedure and the post-transplant follow-up of transplant recipients and living donors.

Transplant services should implement an effective quality management system in order to ensure that the entire operation is compliant (see Chapter 2).

Institutional procedures should be reviewed on a regular basis and whenever modifications are necessary.

Appropriate facilities should be available for grafting/implanting.

7.2 Pre-transplant period

7.2.1 Pre-transplant recipient evaluation

Transplantation of organs, cells and certain tissues requires a multidisciplinary approach. The evaluation process is greatly dependent on the type of recipient and the type of transplant to be performed, the degree of urgency, and the availability of appropriate donors. Evaluation of patients for transplantation should follow established standards for each type
of organ, tissue or cell and should be timely and cost-effective. The pre-transplant evaluation should include a full medical and psychosocial examination and additional diagnostic procedures where relevant.

In relevant cases, further evaluation of transplant recipients should identify potentially important co-morbid conditions and evaluate possible additional risk factors, travel history, and vaccination status. Where appropriate, vaccination should be considered for Hepatitis B. This evaluation should include specific screening and microbiological tests. The testing should be undertaken with the recipient’s informed consent. Potential organ and cell transplant recipients and, where appropriate, tissue transplant recipients, should be tested for a number of diseases.

Recommended tests for potential transplant recipients will depend on the type of transplant. Where relevant it is recommended that appropriate recipient archive samples be maintained.

*a. Indications*

It is recommended that for each type of transplant clearly defined indications be agreed on to ensure equal access and the best use of available grafts. However, the indications for transplantation do not remain constant because advances in medicine, pharmacology and surgical techniques change the prognosis for specific diseases and the outcome of transplant procedures. Therefore indications for transplantation should be reviewed on a regular basis.

*b. Contraindications*

Clinical conditions associated with outcomes so poor as to preclude consideration for transplantation may represent absolute and permanent contraindications to transplantation. Clinical conditions that may adversely affect the outcome of transplantation but do not absolutely preclude it are relative or temporary contraindications. These are a matter for individual clinical judgement which should be fully documented.

7.2.2 *Waiting lists and priorities*

There is an increasing gap between the number of available grafts—organs and patients waiting for transplantation. Defined candidates, with their informed consent, should be put
on a waiting list according to medical urgency criteria and local and/or national rules. Due to
the short time that some organs can be maintained in good condition to be transplanted there
should be a system that ensures that the retrieved organs are allocated to the most
appropriate recipients and that the access to transplantation is justifiable. The waiting list
may be local, regional, national or international. Patients should not be on more than one
waiting list for a specific type of graft.

The waiting lists should be organ specific and, where relevant, can also be tissue and cell
specific. Depending on the local situation certain groups of patients may be prioritised as, for
example, with paediatric, multi-organ recipients or patients in an extremely critical
condition. Generally, recipients of organs from a living donor should fulfil the same
criteria for being placed on the same waiting list as for recipients of cadaveric organs.

a. Immunological priorities

Urgency codes for classification of transplant candidates depend on the type of transplant.
For kidneys, the urgency code for candidates combines aspects of transplantability, medical
urgency and the most recent level of allo-sensitisation. Depending on the policy of a
transplant centre or a national or international organ exchange organisation, highly
immunised transplant candidates may be prioritised.

b. Medical priorities – urgency list

The rules and definitions on priorities and urgency should be public and transparent, and the
mechanisms should ensure equality of access. Defined criteria for priorities and urgency lists
should be established.

c. Follow-up of patients on the waiting list

During the waiting period patients should be regularly re-evaluated. The patient’s condition
may change and this may require alteration to the patient’s waiting list status.
7.2.3 Donor-recipient matching

a. Age and size match
Paediatric organs should preferably be offered to paediatric recipients. Organs from older donors should preferably be used in older recipients. For thoracic and liver transplant recipients matching for body size is an important consideration. Size considerations also pertain to HPC bone marrow (BM) transplantation as this may affect the cell dose. Larger donors can provide higher cell doses.

b. Immunological matching
In relevant potential transplant recipients, particularly some organ and HPC recipients BM patients, ABO blood group as well as HLA investigation is required. In organ transplant patients ABO matching is required, but in some situations can be overridden. Also, good HLA matching between donor and recipient is usually desirable for renal, pancreatic and small bowel transplants, but may not be required for other organ transplants. In HPC donation, HLA considerations may override ABO compatibility. Matching of Rh blood groups is in general not required. The administration of prophylactic anti-D immunoglobulin may be considered in Rh(D) negative females of or below childbearing age who receive a graft from an Rh(D) positive recipient.

Each centre should have an agreed and documented policy describing histocompatibility tests required prior to or following transplantation, the samples to be tested and the interpretation of results. Potential organ transplant candidates should be tested for the presence of HLA-specific antibodies. In highly sensitised patients the specificity of the antibodies should be defined and the patients registered in a shared transplant database to increase the chances of finding a match.

c. Matching concerning serological status of infectious diseases
See Chapter 3 for details.
7.3 Peri-transplant period

7.3.1 Organ transplantation

a. Preoperative assessment
To rule out any new contraindications for transplantation, the preoperative assessment in the transplant unit should be performed by a transplant physician or surgeon and should include detailed medical examination. Pregnancy should be excluded in female patients before any transplant procedure.

b. Surgery
Basic documentation of the recipient procedure should be carried out and the records kept. The operative record should include the warm and cold ischemia time, the type of perfusion and re-perfusion solutions used, evaluation of the re-perfusion of the organ and the intra-operative function of the graft and a description of the surgical technique used.

c. Immunosuppression
Transplant units should have written protocols for induction and maintenance of immunosuppressive therapy as well as the management of rejection and graft-versus-host disease. All protocols or changes should be based on evidence from properly conducted clinical trials.

7.3.2 Tissue transplantation
The decision to use human materials is the responsibility of the transplant surgeon and should be based on established indications and medical standards. Tissues should be obtained from authorised tissue establishments.

7.3.3 Cell transplantation

a. HPC
The HPC transplant team should have written protocols detailing the pre-transplant conditioning therapy of the recipient, processing, purging and manipulation of the graft and the graft-versus-host disease prophylaxis of the recipient after the transplant. This should
include all aspects of recipient care including blood component transfusion support, cytokine
administration, antimicrobial therapy, nutrition, nursing, etc. Records should be maintained
of the graft content, including the enumeration of the stem cells administered.

b. Islet transplantation

Quantity and quality of islet preparations to be transplanted should be documented by the
enumeration of the equivalent islet number, the viability and by an in vitro stimulation test
for insulin release. Appropriate graft parameters should ensure avoidance of acute portal
hypertension and intravascular coagulation in the recipient. *islet transplantation.*

7.4 Post-transplant period

Careful follow-up and documentation of transplant outcomes is a prerequisite for the whole
transplantation process, not only for scientific reasons but mainly because it represents the
final step of the quality chain applied to the whole process. Therefore, in order to allow the
periodical analysis of transplant results, it is mandatory to keep all relevant data related to
the donor, the graft and the recipient follow up. The collection and analysis of these data on
a regular basis will allow evaluation of the effectiveness of the quality programme and the
identification of measures to be adopted for the continuous improvement of the
transplantation programme.

7.4.1 Donor follow-up

a. Living organ donors

Living organ donors should be followed for life to diagnose and treat any late complications
relating to the organ donation.

It is recommended that living donor registries be established to assess donor mortality and
morbidity in post-donation life, to permit tracking of donors and to help in counselling those
who are planning to act as living donors.
b. Living tissue and cell donors

There should be written SOPs to follow-up donors of HPC. For related donors the physician undertaking the assessment of the donor for the bone marrow (BM) or G-CSF mobilised PBPC harvest should be responsible for this. For unrelated donors, follow-up should follow the policies set by the relevant BM donor registry. Where G-CSF is administered, donors should have long-term follow-up, be followed up not only for regular periods in the first year, but in the long term.

Adverse reactions to HPC BM or aphaeresis harvest procedures or administration of cytokines should be documented and reported. This should include any second donations including the harvest of CIT, donor lymphocytes for infusion (DLI).

7.4.2 Recipient follow-up

Post-operative transplant recipient care should be properly defined in SOPs and documented in the recipient notes. It should include, where appropriate:

- a regular general medical examination, and when required, further graft and organ-specific diagnostic procedures;
- functional parameters of the graft;
- prevention, diagnosis and treatment of rejection, graft-versus-host disease, infections, malignancies, and other diseases;
- adverse reactions;
- detection of residual disease and secondary disease processes;
- appropriate registries of the graft recipients, respecting national regulations and patients’ privacy should be maintained.

It should be noted that therapies involving long living, sometimes proliferating cells can have long-term effects, and follow-up should take this into account.
7.4.3 Adverse reactions and vigilance

Records should be maintained of all reports of complaints or adverse reactions to any treatment related to the transplant procedure. Copies of written reports should be forwarded to and maintained by the procurement organisation, tissue establishments and transplant centres, as appropriate, according to existing regulations. Severe adverse events and reactions should be reported immediately to competent authorities. According to the national regulations, a transplant team and a tissue establishment who received material from the same donor should be notified.

7.5 Use of organs, tissues and cells for purposes other than transplantation

This document is primarily concerned with the quality and safety of organs, tissues and cells used for therapeutic purposes. However, it is recognised that there may be some material which for some reason or another cannot be transplanted, and which it would be entirely appropriate to release for other purposes, such as bona fide medical research, toxicological testing or education. This guide recognises that such activities can be legitimate provided that a presumed or informed donor or family consent is obtained. Such activities have potential benefit for individual patients and society, both in the short and long term. Some of these activities, such as medical research, are subject to specific requirements under other protocols.

An objective of this guide is to ensure that human material retrieved primarily for transplantation but not subsequently used for the purpose is not then used inappropriately or unethically. Only if appropriate (informed or presumed) consent for research or other use has been obtained should any organs or tissues, or cells which may become surplus or which are considered inappropriate for therapeutic needs, be released according to national regulations. Organs, tissues and cells for which only consent for purposes of transplantation has been obtained, should be disposed of according to national regulations.
Appendices
Appendix 1 – SP-SQA group participants

Dr. Margarida Amil DIAS  
Dept of Transplantation  
Hospital S. António  
Largo Abel Salaza, 4000 Porto, Portugal  
E-mail: margarida.amil@mail.telepac.pt

Dr. Rachel GREEN  
West of Scotland Blood Transfusion Service  
25 Shelley Road  
c/o Gartnavel General Hospital  
Glasgow, G12 0XB, UK  
E-mail: rachelhagreen@hotmail.com; rachel.green@snbts.csa.scot.nhs.uk

Dr. Andrew HADLEY BSc., DPhil,  
National Stem Cell Services Manger,  
National Blood Service,  
Southmead Road,  
Bristol BS10 5ND, UK  
E-mail: andrew.hadley@nbs.nhs.uk

Dr. Ján KOLLER, M.D., CSc  
Chair of the SP-SQA Group  
Associate Professor of Surgery  
Head, Center for Burns and Reconstructive Surgery  
Central Tissue Bank  
University Hospital Bratislava workplace Ruzinov Ruzinovska 6  
821 07 Bratislava, Slovak Republic  
E-mail: koller@nspr.sk, jankoller@hotmail.com
Prof. Dr. Werner LAUCHART  
Deutsche Stiftung Organtransplantation  
Organisationszentrale Baden-Württemberg  
Friedrich Strasse 10  
70174 Stuttgart, Germany  
E-mail: werner.lauchart@dso.de

Dr. Bernard LOTY  
Directeur  
Direction médicale et Scientifique  
Agence de la Biomédecine  
1 avenue du Stade de France  
93212 Saint-Denis La Plaine Cedex  
E-mail: bernard.loty@biomedecine.fr  
Site web: www.agence-biomedecine.fr

Dr. Marti MANYALICH  
Hospital Clinic Barcelona  
Transplant Services Foundation  
Villarroel, 170  
08036 Barcelona, Spain  
E-mail: mmanya@clinic.ub.es

Dr. Jose OBERHOLZER, MD  
Associate Professor of Surgery and Bioengineering  
Director Cell and Pancreas Transplantation  
Division of Transplantation (MC 958)  
840 South Wood Street CSB (Rm 402)  
Chicago, Illinois 60612  
USA  
E-mail: jober@uic.edu
Dr Antony PETKOV
Transplantation organs and tissues coordinator
8, “Bialo more” str.
Sofia 1000, Bulgaria
E-mail: antony_petkov@yahoo.com

Dr. Giuseppe PICCOLO
Centro Interregionale di Riferimento
Nord Italy Transplant Program
V.F.Sforza 35, Milano, Italy
E-mail: tessuti@policlinico.mi.it; info@nitp.org

Dr Kaija SALMELA
Head of Renal Transplant Unit
Kidney Transplant Unit
Helsinki University Hospital
Surgical Hospital
Kasarmikatu 11-13
SF-00130 Helsinki, Finland
E-mail: kaija.salmela@hus.fi

M. Dr. László SZÖNYI MD
Semmelweis University
I.st.Department of Pediatrics
H-1083 Budapest
Bókay János u.53., Hungary
email: szolasz@gyer1.sote.hu

Dr. Esteve TRIAS
Hospital Clinic Barcelona
Transplant Coordination Unit
C/Villarroel, 170
08036 Barcelona, Spain
E-mail: etrias@clinic.ub.es
Mr C. WASSENAAR, Ph.D, M.D.
Centre for Biological Medicines and Medical Technology
National Institute for Public Health and the Environment
P.O. Box 1
3720 BA Bilthoven, The Netherlands
E-mail: claes.wassenaar@rivm.nl

Mr Victor ZOTA
Str. Eminescu n°224-226
Setor 2
Bucuresti, Romania
E-mail: victor_zota@hotmail.com; ant.msr@gmail.com

European Commission

Mr. Eduardo FERNANDEZ ZINCKE
European Commission
Directorate-General Health and Consumer Protection
Public Health and Risk Assessment Directorate
Unit C6 Health Measures
Batiment J. Monnet, Rue A. De Gasperi
L-2920 Luxembourg
E-mail: Eduardo.Fernandez-Zincke@cec.eu.int

European Association of Tissue Banks (EATB)

Dr. Rüdiger von VERSEN, MD, DMSc
Medical Director
German Institute for Cell and Tissue Replacement (DIZG)
Koepenicker Str. 325, Bldg. 42
D-12555 Berlin, Germany
E-mail: R_vonVersen@dizg.de
Web: http://www.dizg.de
European Society for Organ Transplantation (ESOT)

Prof. Jan LERUT, MD. PhD  
Dept. of Surgery  
University Medical Center Groningen UMCG  
P.O. Box 30.001  
NL-9700 RB Groningen  
The Netherlands  
E-mail: j.t.uildriks@chir.umcg.nl  
lerut@chir.ucl.ac.be

World Health Organisation (WHO)

Dr. Luc NOEL MD  
Coordinator  
Clinical Procedures  
Essential Health Technologies  
Health Technology and Pharmaceuticals  
World Health Organization  
20 avenue Appia  
1211 Geneva 27, Switzerland  
E-mail: noell@who.int

European Group for Blood and Marrow Transplantation (EBMT)

Dr Diana SAMSON  
35 Ewelme Road  
London SE23 3BQ, UK  
E-mail: DrDianaSamson@aol.com
Co-ordination

Alina TATARENKO
Administrative Officer
Health Division
Department of Health and of the Partial Agreement
in the Social and Public Health Field
Directorate General III – Social Cohesion
Council of Europe
67075 Strasbourg Cedex, France
Tel: +33388412847
Fax: +33388412726
E-mail: alina.tatarenko@coe.int

Sophie-Marie LE GUILLOUX
Assistant
Health Division
Department of Health and of the Partial Agreement
in the Social and Public Health Field
Directorate General III – Social Cohesion
Council of Europe
67075 Strasbourg Cedex, France
Tel: +33390214081
Fax: +33388412726
E-mail: sophie-marie.leguilloux@coe.int
Appendix 2 – List of relevant standards/guidelines

Standards

1. Standards for Tissue Banking, AATB (American Association of Tissue Banks)
2. Common Standards for Musculo-Skeletal Tissue Banking, European Association of Tissue Banks & European Association of Musculo-Skeletal Transplantation
5. General Standards for Tissue Banking, European Association of Tissue Banks
6. The Medical Standards of the Eye Bank Association of America
7. The Medical Standards of the European Eye Bank Association
8. JACIE standards on the EBMT website:

Council of Europe publications:

http://www.coe.int/T/E/Social_Cohesion/Health/Activities/Organ_transplantation/:

9. Recommendation No. R (94) 1 on human tissue banks, 1994
10. Resolution (78) 29 on harmonisation of legislations of member states relating to removal, grafting and transplantation of human substances, 1978
11. Recommendation No. R (97) 16 on liver transplantation from living related donors, 1997
14. Additional Protocol to the Convention for the Protection of Human Rights and Dignity with regard to the Application of Biology and Medicine, on Transplantation of Organs and Tissues of Human Origin, 2002
15. Standardisation of organ donor screening to prevent transmission of neoplastic diseases, 1997
16. State of the art report on serological screening methods for the most relevant microbiological diseases of organ and tissue donors, 1997
17. Solutions for organ preservation, EDQM (European Directorate for the Quality of Medicines, European Pharmacopoeia) monograph, 1997

18. Report on Cellular Immune Therapies, Council of Europe
   http://www.coe.int/T/E/Social_Cohesion/Health/Activities/Organ_Transplantation/

European Union publications:

2. The Rules Governing Medicinal Products in the European Union, 2004:
   http://pharmacos.eudra.org/F2/eudralex/index.htm
Appendix 3 – Example of the evaluation of donor risk factors for transmissible diseases

• Men who have had sex with another man in the preceding 12 months.
• Persons who report non-medical intravenous, intramuscular, or subcutaneous injection of drugs in the preceding 12 months.
• History of chronic haemodialysis.
• Men and women who have engaged in sex in exchange for money or drugs in the preceding 12 months.
• Persons with haemophilia or related clotting disorders who have received human-derived clotting factor concentrates.
• Persons who were sexual partners of persons having a HIV or Hepatitis B or C history, manifestations, or risk factors previously described, in the preceding 12 months.
• Percutaneous exposure or contact with an open wound, non-intact skin, or mucous membrane to blood thought to be at high risk for carrying HIV or hepatitis in the preceding 12 months.
• Inmates of correctional systems in preceding 12 months.
• Diagnosed or treated for syphilis or gonorrhoea in preceding 12 months.
• A potential tissue donor who has received a blood transfusion within 12 months prior to death may only be accepted as a tissue donor after individual approval from the responsible person.
• The donor is not eligible if in a deferral status of any Blood Services Donor Deferral Register. The local blood centre(s) should be checked each time if possible (blood donor card available).
• Tattoo, ear piercing, body piercing, and/or acupuncture, unless by sterile, non-reused needle or equipment, in the preceding 12 months.
• Children born to mother with HIV infection or with HIV behavioural risk unless HIV infection can be definitively excluded in the child. Such children under 18 months of age or who have been breast-fed within the last 12 months should not be accepted as donors regardless of their HIV test results.
• *history of recent immunisation with live vaccines*

• *history of travel to areas with endemic transmissible diseases such as malaria, trypanosomiasis, rabies, WNV, etc. (see www.CDC.gov)*
Appendix 4 – Definitions

Adverse event: any undesirable or unintentional event associated with the procurement, testing, processing, storage and distribution of organs, or tissues and cells.

Allocation: assignment and distribution of organs or tissues or cells.

Allogeneic use: organs, tissues or cells transplanted from one person to another.

Allograft: graft transplanted between two genetically different individuals of the same species.

Anti-HBe: Hepatitis B core antibody.

Aseptic processing: whereby the tissue, container and closure are bacteria-free or subject to sterilisation separately and then brought together.

Audit: documented review of procedures, records, personnel functions, equipment, materials, facilities and/or vendors in order to evaluate adherence to written SOPs, standards or government laws and regulations.

Autologous use: cells or tissues removed from and transplanted back to the same person.

Batch (also lot): defined quantity of tissue produced.

BM: bone marrow, haematopoietic progenitor cells (HPCs) aspirated from the iliac crests, sternum or other bones.

CB: cord blood.

Cells: individual cells or collections of cells when not bound by any form of connective tissue.

CIT: cellular immune therapies which involve the collection, manipulation, and administration of, for example, lymphocytes, natural killer cells, macrophages, dendritic cells or (modified) tumour cells with the intended purpose of modulating an immune response in the recipient.

Clean, non-sterile: use of methods and techniques that keep microbial contamination of the material collected at a minimum level.

CMV: cytomegalovirus.

Container: an enclosure for one finished unit of transplantable cells, tissue or organ.

Cord blood: haematopoietic progenitor cells collected from placental and umbilical cord blood vessels after the umbilical cord is clamped.

CPK: creatinine phosphokinase.

CPK-MB: creatinine phosphokinase-MB fraction.
**Cross-contamination:** transfer of micro-organisms from one material to another material.

**Disinfection:** a process that reduces the number of viable micro-organisms, but does not necessarily destroy all microbial forms, such as spores and viruses.

**Distribution:** transportation and delivery of organs, tissues or cells for storage, processing or use in recipients.

**Donor:** every human source, whether living or deceased, of organs, tissues or cells.

**Donor selection:** the evaluation of information about a potential donor to determine whether the donor meets qualifications specified in the SOPs.

**End user:** health care practitioner who performs transplantation procedures.

**Facility:** any area used in the procurement, processing, testing, storage or distribution of tissue and tissue components.

**G-CSF:** granulocyte colony stimulating factor.

**GLP:** good laboratory practice

**GMP:** good manufacturing practice.

**HBV:** Hepatitis B Virus.

**HCV:** Hepatitis C Virus.

**HIV:** Human Immunodeficiency Virus.

**HLA:** Human Leukocyte Antigen.

**HPC:** Haematopoietic progenitor cell.

**HTLV1/2:** Human T cell-leukaemia virus 1/2.

**Implantation/grafting:** the process of inserting an organ, piece of tissue or cells into a recipient.

**Informed consent:** a procedure whereby information concerning the donation process is presented to the donor or to the donor’s next of kin, without coercion, with an opportunity for them to ask questions, after which specific approval is documented.

**Ischaemia times:** warm ischaemia time refers to the period between circulatory arrest and commencement of cold storage. Cold ischaemia time refers to the period of cold storage.

**Labelling:** includes steps taken to identify the material and to attach the appropriate labels to the container or package so they are clearly visible through the immediate carton, receptacle or wrapper. This should include adequate directions for the safe use of the graft.

**Manipulation:** an in vitro procedure that selectively removes, enriches, expands or functionally alters haematopoietic progenitor cells (HPCs).
Mother: the birth mother who carries the infant to term. When a surrogate mother carries the infant to term, the egg donor should be considered the mother for the purpose of genetic information, while the birth mother should be considered the mother for purposes of transmissible disease testing.

NAT: nucleic acid testing

Organ: a differentiated and vital part of the human body, formed by different tissues, that maintains its structure, vascularisation and capacity to develop physiological functions with an important level of autonomy.

Package insert: written material accompanying a tissue graft bearing further information about the tissue, directions for use and any applicable warnings.

Packaging (tissue package): additional wrapping used to protect one or more tissue containers during transit.

PBPC: peripheral blood progenitor cells collected from the peripheral blood.

Pooling: the physical contact or mixing of cells or tissue from two or more donors in a single container.

Preservation: the use of chemical agents, alterations in environmental conditions or other means during processing to prevent or retard biological or physical deterioration of organs, tissues or cells.

Presumed consent: add from CoE Rec

Procedure: a series of technical steps precisely followed in a defined order.

Processing: all operations involved in the preparation, manipulation, preservation and packaging of organs, tissues or cells for transplantation.

Procurement: a process by which the donated organs, tissue or cells become available.

Proficiency testing: a specific tool for monitoring the competency (performance) of personnel in carrying out their allocated tasks.

Quality: degree to which a set of characteristics fulfil requirements.

Quality assurance (QA): describes the actions, planned and performed, to provide confidence that all systems and elements that influence the quality of the product are working as expected individually and collectively, may also encompass GLP.

Quality control: part of quality management focused on fulfilling quality requirements. This is the part of GMP which is concerned with sampling, specifications and testing and with the organisation, documentation and release procedures which ensure that the necessary and
relevant tests are actually carried out and that materials are not released for use until their
quality has been judged to be satisfactory.

**Quality improvement:** describes the actions planned and performed to develop a system to
review and improve the quality of a product or process.

**Quality management:** the co-ordinated activities to direct and control an organisation with
regard to quality. A general term encompassing all aspects which ensure the final quality of
organs, tissues and cells.

**Quarantine:** the status of retrieved tissue or cells or packaging material, or tissue isolated
physically or by other effective means while awaiting a decision on their release or
rejection.

**Recipient:** the person into whom an organ, tissue or cells is/are grafted/implanted.

**Retrieval:** the removal of organs, tissues or cells from a donor for the purpose of
transplantation.

**Self assessment:** a comprehensive and systematic review of the organisation’s activities and
results referenced against the QMS or a model of excellence, which can thus help identify
areas requiring improvement.

**Serious adverse event:** any untoward occurrence associated with the procurement, testing,
processing, storage and distribution of organs, tissues and cells that might lead to the
transmission of a communicable disease, to death or life-threatening, disabling or
incapacitating conditions for patients or which results in, or prolongs, hospitalisation or
morbidity.

**Serious adverse reaction:** an unintended response, including a communicable disease, in the
donor or in the recipient associated with the procurement or transplantation of organs,
tissues and cells that is fatal, life-threatening, disabling, incapacitating or which results in, or
prolongs, hospitalisation or morbidity.

**SOP:** Standard Operating Procedure: written instructions which document all steps in
procedures

**Sterilisation:** a physical or chemical process validated to destroy, inactivate or to reduce
micro-organisms to a sterility assurance level of 10-6.

**Storage:** maintenance of tissues and cells in a state ready for distribution.

**Tissue:** all constituent parts of the human body formed by cells.

**Tissue bank:** see tissue establishment.

**Tissue container:** wrapping system ensuring the integrity and sterility of tissues.
**Tissue establishment (TE):** a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells.

**Traceability:** the ability to identify the organ/tissue/cell during any step between its donation, collection, processing, testing, storage and distribution whether to recipient or disposal. It implies the capacity to identify the donor and the medical facility receiving the organ/tissue, and at the medical facility, the ability to identify the recipient. *This traceability shall also apply to all relevant data relating to products and materials coming into contact with these organs, tissues and cells.*

**Transplantation:** the process of reconstituting a function by transferring equivalent organs, tissues or cells to a recipient. Transplantation may be from one person to another (allogeneic) or from a person to him or herself (autologous).

**Validation:** refers to establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes. A process is validated to evaluate the performance of a system with regard to its effectiveness based on intended use.

**Vascularised organs:** any part of a human body consisting of a vascularised structured arrangement of tissues which, if wholly removed, cannot be replicated by the body.
Appendix 5 – Additional protocol to the convention on human rights and biomedicine, on transplantation of organs and tissues of human origin

Formally approved by the Committee of Ministers in
Strasbourg, 24 January 2002

Preamble

The member States of the Council of Europe, the other States and the European Community signatories to this Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (hereinafter referred to as “Convention on Human Rights and Biomedicine”),

Considering that the aim of the Council of Europe is the achievement of greater unity between its members and that one of the methods by which this aim is pursued is the maintenance and further realisation of human rights and fundamental freedoms;

Considering that the aim of the Convention on Human Rights and Biomedicine, as defined in Article 1, is to protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine;

Considering that progress in medical science, in particular in the field of organ and tissue transplantation, contributes to saving lives or greatly improving their quality;

Considering that transplantation of organs and tissues is an established part of the health services offered to the population;

Considering that, in view of the shortage of organs and tissues, appropriate action should be taken to increase organ and tissue donation, in particular by informing the public of the importance of organ and tissue transplantation and by promoting European co-operation in
this field;

Considering moreover the ethical, psychological and socio-cultural problems inherent in the transplantation of organs and tissues;

Considering that the misuse of organ and tissue transplantation may lead to acts endangering human life, well being or dignity;

Considering that organ and tissue transplantation should take place under conditions protecting the rights and freedoms of donors, potential donors and recipients of organs and tissues and that institutions must be instrumental in ensuring such conditions;

Recognising that, in facilitating the transplantation of organs and tissues 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 and tissue procurement, exchange and allocation activities;

Taking into account previous work of the Committee of Ministers and the Parliamentary Assembly of the Council of Europe in this field;

Resolving to take such measures as are necessary to safeguard human dignity and the rights and fundamental freedoms of the individual with regard to organ and tissue transplantation,

Have agreed as follows:

Chapter I – Object and scope

Article 1 – Object

Parties to this Protocol shall protect the dignity and identity of everyone and guarantee, without discrimination, respect for his or her integrity and other rights and fundamental freedoms with regard to transplantation of organs and tissues of human origin.
Article 2 – Scope and definitions

1. This Protocol applies to the transplantation of organs and tissues of human origin carried out for therapeutic purposes.

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

3. The Protocol does not apply:

   a. to reproductive organs and tissue;
   b. to embryonic or foetal organs and tissues;
   c. to blood and blood derivatives.

4. For the purposes of this Protocol:

   – 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 and storage;

   – subject to the provisions of Article 20, the term “removal” refers to removal for the purposes of implantation.

Chapter II – General provisions

Article 3 – Transplantation system

Parties shall guarantee that a system exists to provide equitable access to transplantation services for patients.

Subject to the provisions of Chapter III, organs and, where appropriate, tissues shall be allocated only among patients on an official waiting list, in conformity with transparent, objective and duly justified rules according to medical criteria. The persons or bodies responsible for the allocation decision shall be designated within this framework.
In case of international organ exchange arrangements, the procedures must also ensure justified, effective distribution across the participating countries in a manner that takes into account the solidarity principle within each country.

The transplantation system shall ensure the collection and recording of the information required to ensure traceability of organs and tissues.

**Article 4 – Professional standards**

Any intervention in the field of organ or tissue transplantation must be carried out in accordance with relevant professional obligations and standards.

**Article 5 – Information for the recipient**

The recipient and, where appropriate, the person or body providing authorisation for the implantation shall beforehand be given appropriate information as to the purpose and nature of the implantation, its consequences and risks, as well as on the alternatives to the intervention.

**Article 6 – Health and safety**

All professionals involved in organ or tissue transplantation shall take all reasonable measures to minimise the risks of transmission of any disease to the recipient and to avoid any action which might affect the suitability of an organ or tissue for implantation.

**Article 7 – Medical follow-up**

Appropriate medical follow-up shall be offered to living donors and recipients after transplantation.
Article 8 – Information for health professionals and the public

Parties shall provide information for health professionals and for the public in general on the need for organs and tissues. They shall also provide information on the conditions relating to removal and implantation of organs and tissues, including matters relating to consent or authorisation, in particular with regard to removal from deceased persons.

Chapter III – Organ and tissue removal from living persons

Article 9 – General rule

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

Article 10 – Potential organ donors

Organ removal from a living donor may be carried out for the benefit of a recipient with whom the donor has a close personal relationship as defined by law, or, in the absence of such relationship, only under the conditions defined by law and with the approval of an appropriate independent body.

Article 11 – Evaluation of risks for the donor

Before organ or tissue removal, appropriate medical investigations and interventions shall be carried out to evaluate and reduce physical and psychological risks to the health of the donor.

The removal may not be carried out if there is a serious risk to the life or health of the donor.

Article 12 – Information for the donor

The donor and, where appropriate, the person or body providing authorisation according to
Article 14, paragraph 2, of this Protocol, shall beforehand be given appropriate information as to the purpose and nature of the removal as well as on its consequences and risks.

They shall also be informed of the rights and the safeguards prescribed by law for the protection of the donor. In particular, they shall be informed 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 or tissue removal or subsequent transplantation procedures.

**Article 13 – Consent of the living donor**

Subject to Articles 14 and 15 of this Protocol, an organ or tissue may be removed from a living donor only after the person concerned has given free, informed and specific consent to it either in written form or before an official body.

The person concerned may freely withdraw consent at any time.

**Article 14 – Protection of persons not able to consent to organ or tissue removal**

1. No organ or tissue removal may be carried out on a person who does not have the capacity to consent under Article 13 of this Protocol.

2. Exceptionally, and under the protective conditions prescribed by law, the removal of regenerative tissue from a person who does not have the capacity to consent may be authorised provided the following conditions are met:

   i. there is no compatible donor available who has the capacity to consent;

   ii. the recipient is a brother or sister of the donor;

   iii. the donation has the potential to be life-saving for the recipient;

   iv. the authorisation of his or her representative or an authority or a person or body provided for by law has been given specifically and in writing and with the approval
of the competent body;

v. the potential donor concerned does not object.

Article 15 – Cell removal from a living donor

The law may provide that the provisions of Article 14, paragraph 2, indents ii and iii, shall not apply to cells insofar as it is established that their removal only implies minimal risk and minimal burden for the donor.

Chapter IV – Organ and tissue removal from deceased persons

Article 16 – Certification of death

Organs or tissues shall not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law.

The doctors certifying the death of a person shall not be the same doctors who participate directly in removal of organs or tissues from the deceased person, or subsequent transplantation procedures, or having responsibilities for the care of potential organ or tissue recipients.

Article 17 – Consent and authorisation

Organs or tissues shall not be removed from the body of a deceased person unless consent or authorisation required by law has been obtained.

The removal shall not be carried out if the deceased person had objected to it.

Article 18 – Respect for the human body

During removal the human body must be treated with respect and all reasonable measures shall be taken to restore the appearance of the corpse.
Article 19 – Promotion of donation

Parties shall take all appropriate measures to promote the donation of organs and tissues.

Chapter V – Implantation of an organ or tissue removed for a purpose other than donation for implantation

Article 20 – Implantation of an organ or tissue removed for a purpose other than donation for implantation

1. When an organ or tissue is removed from a person for a purpose other than donation for implantation, it may only be implanted if the consequences and possible risks have been explained to that person and his/her informed consent, or appropriate authorisation in the case of a person not able to consent, has been obtained.

2. All the provisions of this Protocol apply to the situations referred to in paragraph 1, except for those in Chapter III and IV.

Chapter VI – Prohibition of financial gain

Article 21 – Prohibition of financial gain

1. The human body and its parts shall not, as such, give rise to financial gain or comparable advantage.

The aforementioned provision shall not prevent 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 the related medical examinations;
- payment of a justifiable fee for legitimate medical or related technical
services rendered in connection with transplantation;

- compensation in case of undue damage resulting from the removal of organs or tissues from living persons.

2. Advertising the need for, or availability of, organs or tissues, with a view to offering or seeking financial gain or comparable advantage, shall be prohibited.

**Article 22 – Prohibition of organ and tissue trafficking**

Organ and tissue trafficking shall be prohibited.

**Chapter VII – Confidentiality**

**Article 23 – Confidentiality**

1. All personal data relating to the person from whom organs or tissues have been removed and those relating to the recipient shall be considered to be confidential. Such data may only be collected, processed and communicated according to the rules relating to professional confidentiality and personal data protection.

2. The provisions of paragraph 1 shall be interpreted without prejudice to the provisions making possible, subject to appropriate safeguards, the collection, processing and communication of the necessary information about the person from whom organs or tissues have been removed or the recipient(s) of organs and tissues in so far as this is required for medical purposes, including traceability, as provided for in Article 3 of this Protocol.

**Chapter VIII – Infringements of the provisions of the Protocol**

**Article 24 – Infringements of rights or principles**

Parties shall provide appropriate judicial protection to prevent or to put a stop to an unlawful infringement of the rights and principles set forth in this Protocol at short notice.
Article 25 – Compensation for undue damage

The person who has suffered undue damage resulting from transplantation procedures is entitled to fair compensation according to the conditions and procedures prescribed by law.

Article 26 – Sanctions

Parties shall provide for appropriate sanctions to be applied in the event of infringement of the provisions contained in this Protocol.

Chapter IX – Co-operation between Parties

Article 27 – Co-operation between Parties

Parties shall take appropriate measures to ensure that there is efficient co-operation between them on organ and tissue transplantation, *inter alia* through information exchange.

In particular, they shall undertake appropriate measures to facilitate the rapid and safe transportation of organs and tissues to and from their territory.

Chapter X – Relation between this Protocol and the Convention, and re-examination of the Protocol

Article 28 – Relation between this Protocol and the Convention

As between the Parties, the provisions of Articles 1 to 27 of this Protocol shall be regarded as additional articles to the Convention on Human Rights and Biomedicine, and all the provisions of that Convention shall apply accordingly.

Article 29 – Re-examination of the Protocol

In order to monitor scientific developments, the present Protocol shall be examined within
the Committee referred to in Article 32 of the Convention on Human Rights and Biomedicine no later than five years from the entry into force of this Protocol and thereafter at such intervals as the Committee may determine.

Chapter XI – Final clauses

Article 30 – Signature and ratification

This Protocol shall be open for signature by Signatories to the Convention. It is subject to ratification, acceptance or approval. A Signatory may not ratify, accept or approve this Protocol unless it has previously or simultaneously ratified, accepted or approved the Convention. Instruments of ratification, acceptance or approval shall be deposited with the Secretary General of the Council of Europe.

Article 31 – Entry into force

1. This Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date on which five States, including at least four member States of the Council of Europe, have expressed their consent to be bound by the Protocol in accordance with the provisions of Article 30.

2. In respect of any signatory which subsequently expresses its consent to be bound by it, the Protocol shall enter into force on the first day of the month following the expiration of a period of three months after the date of the deposit of the instrument of ratification, acceptance or approval.

Article 32 – Accession

1. After the entry into force of this Protocol, any State which has acceded to the Convention may also accede to this Protocol.

2. Accession shall be effected by the deposit with the Secretary General of the Council of Europe of an instrument of accession which shall take effect on the first day of the month
following the expiration of a period of three months after the date of its deposit.

**Article 33 – Denunciation**

1. Any Party may at any time denounce this Protocol by means of a notification addressed to the Secretary General of the Council of Europe.

2. Such denunciation shall become effective on the first day of the month following the expiration of a period of three months after the date of receipt of such notification by the Secretary General.

**Article 34 – Notification**

The Secretary General of the Council of Europe shall notify the member States of the Council of Europe, the European Community, any Signatory, any Party and any other State which has been invited to accede to the Convention of:

a. any signature;

b. the deposit of any instrument of ratification, acceptance, approval or accession;

c. any date of entry into force of this Protocol in accordance with Articles 31 and 32;

d. any other act, notification or communication relating to this Protocol.

In witness whereof the undersigned, being duly authorised thereto, have signed this Protocol.

Done at Strasbourg, this 24th day of January 2002, in English and in French, both texts being equally authentic, in a single copy which shall be deposited in the archives of the Council of Europe. The Secretary General of the Council of Europe shall transmit certified copies to each member State of the Council of Europe, to the non-member States which have participated in the elaboration of this Protocol, to any State invited to accede to the Convention and to the European Community.