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from :	the Secretary-General of the European Commission signed by Mr Sylvain BISARRE, Director
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to :	Mr Javier SOLANA, Secretary-General/High Representative
Subject :	Proposal for a Directive of the European Parliament and of the Council on setting standards of quality and safety for the donation, procurement, testing, processing, storage and distribution of human tissues and cells

Delegations will find attached Commission document COM(2002) 319 final.

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COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 19.6.2002
COM(2002) 319 final

2002/0128(COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on setting standards of quality and safety for the donation, procurement, testing, processing, storage, and distribution of human tissues and cells

(Presented by the Commission)

EXPLANATORY MEMORANDUM

INTRODUCTION

1. Each year in Europe, hundreds of thousands of patients undergo some form of therapeutic treatment based on the use of tissues and cells of human origin. Employment of these substances in the delivery of health care now goes beyond traditional transplants or implants into another human (allograft), to their incorporation into or combined with medical devices, and as the basis for services or products derived through biotechnology. While the therapeutic value of human allografts has been recognised for several decades, the increased number of implants as well as medical indications demands that requirements to ensure the quality and safety of human tissues and cells for clinical use be established in the European Union

2. Tissues are a functional group of cells, which may be transplanted or implanted as viable cells, or otherwise preserved, fixed, or altered. They include: bone and musculoskeletal elements (e.g. cartilage, tendons, fascias), cardiovascular tissues (e.g. arteries, veins, heart valves), ocular tissue (e.g. cornea, sclera), nerve cells, skin, brain cells, foetal tissue, reproductive cells (e.g. semen, sperm, ova) and stem cells (i.e. haematopoietic progenitor cells obtained from bone marrow, umbilical cord and peripheral circulation). As appropriate, these tissues and cells are used not only in reconstructive surgery such as corneal and hip replacement but also in the treatment of diseases such as cancer and diabetes, and increasingly in reproductive medicine. Advances in biotechnology have resulted in the production of tissue-derived products such as cultured allogeneic cells, engineered structural tissues, and constituent parts of medical devices. All these tissues or cells, which are frequently acquired through cross-border exchanges, come from donors who may be living or deceased.

3. Statistics related to the transplant of some of these human substances reflect their increasing importance to the health care delivery system. In the United States, the number of bone grafts increased 140% from 302,548 to 750,000 between 1992 and 1999. In Europe, the transplant of haematopoietic progenitors increased from less than 4,000 in 1990 to 18,720 in 1999. In 1998, the replacement of heart valves with human allografts numbered 3,412. Today, cornea transplantation in Spain amounts to more than 60 transplants per million population and more than 70 in France.

4. In order to increase public confidence in the use of human tissues and cells for application in the human body, it is essential, therefore, that EU provisions should ensure their quality and safety. Article 152 of the Treaty has provided the European Community (EC) with an opportunity, as well as an obligation, to implement binding measures laying down high standards of quality and safety for the use of blood, organs, and substances of human origin.

5. Increased therapeutic use of substances of human origin and the recognition that they can transmit diseases have led to extensive discussion not only on the need for increased safety measures but also on the associated ethical issues. This latter aspect was the subject of considerable debate during deliberations on the European

Commission's proposal for a Directive on *in vitro* diagnostic medical devices[1]. Opposition to the inclusion of human tissues, which are frequently an integral component of medical devices, in the Directive was based on lack of control, during procurement, of the tissues and cells used as starting material; lack of authorisation for and inspection of manufacturers or tissue banks; non-binding application of standards implied by the Directive without common compulsory specifications; and the existence of over 50 notified bodies in Europe expected to assess product conformity, without scientific level control. The Directive that was ultimately adopted[2] was restricted to substances of human origin rendered non-viable, with most human products remaining unregulated.

6. In 1998, the European Group on Ethics in Science and New Technologies to the European Commission (EGE) confirmed that there was 'the urgent need to regulate the conditions under which human tissues circulate within the European market'[3]. Four aspects were stressed in their report:

- the ethical imperative to protect health. As no substance of human origin is free from the risk of disease transmission, 'tissues, in particular those intended for transplantation to third parties or for the preparation of pharmaceutical specialities, must undergo advance testing to provide maximum health guarantees in accordance with the 'state of the art'';
- the integrity of the human body. This should be ensured when procuring tissues from an individual, whether living or dead;
- the prior, informed, and free consent of the person concerned. Before procurement of human tissues, as a principle the donor's consent must have been given on the basis of information provided in as clear and precise lay terms as possible; and
- The protection of identity. This requires that, in the interests of anonymity, any disclosure of information that could identify either the donor or recipient must be prohibited. In general, the donor should not know the identity of the recipient, nor vice versa – a requirement to prevent possible discrimination.

7. The EGE also noted that anonymous and free tissue donation basically remains a voluntary act of solidarity. People in each Member State should be encouraged to donate tissues in this spirit, thereby promoting shared aims and increasing the availability of substances of human origin in Europe. The EGE also discussed: the role and responsibilities of tissue banks and their profit or non-profit character; equitable access to the therapeutic opportunities afforded by the use of human tissues; and the need for tissue imports from third countries to be subject to at least equivalent ethical and health requirements. This proposal for a Directive reflects the recommendations put forth by the EGE.

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1 Proposal for a European Parliament and Council Directive on in vitro diagnostic medical devices. COM (95) 130 Final. COD (95) 0013. OJ No C 172, 07.07.1995, p.21

2 Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices. OJ L 331, 07.12.1998, p.1-37.

3 'Ethical aspects of human tissue banking'. Opinion of the European Group on Ethics in Science and New Technologies to the European Commission. No. 11, 21 July 1998. 11p.

8. While most Member States have adopted legislation to control the ethical aspects of donor protection (mainly in the area of organ transplantation), many have yet to agree upon rules covering quality, safety or the use of tissues and cells. An informal survey on existing regulations in the Member States carried out in 2000[4] confirmed that considerable discrepancies exist in the coverage with only those aspects related to donor protection addressed to date by nearly all of them. Specific rules for the authorisation for and inspection of tissue procurement and banking activities are lacking in the majority, as are regulations for determining donor suitability and the importation of human substances. The percentages of Member States that have regulations in place covering different topics are illustrated in Tables 1 to 3.

9. During a meeting convened under the Portuguese Presidency in Porto in June 2000, experts in the areas of tissues and cells analysed the regulatory situation in Europe and concluded that there is an urgent need for an EC Directive on the safety and quality of these human substances. Subsequently, experts and official representatives of the Member States arrived at a similar conclusion at a Conference co-organised by the European Commission and the Spanish Presidency in Malaga in February 2002. They supported the idea of developing an EC Directive setting high standards of safety and quality for the procurement, testing, processing, storage, and distribution of human tissues and cells in order to ensure a high level of human health protection in the European Union. They also provided specific orientations for the development of such an initiative, which received a general welcome in an EU Ministerial Seminar that immediately followed the Malaga Conference.

SCOPE AND OBJECTIVES

10. For the first three steps of their use (donation, procurement, and testing), this proposal for a Directive covers all tissues and cells of human origin for application to the human body, except blood and blood products, tissues and cells used as an autologous graft within the same surgical procedure and organs, but including starting materials for tissue and cell derived manufactured products. However, autologous cells used for medicinal products are not covered by this Directive. Tissues and cells used for research purposes would be covered when administered to the human body, but not when used for research *in vitro* or in animal models. The further steps of their use (processing, preservation, storage, and distribution) are covered if the tissues and cells are intended for transplantation.

Donation, procurement, and testing of all human tissues and cells for application to the human body.

11. This proposal for a Directive on human tissues and cells aims to cover all human cells and tissues, which are used for application to the human body, during the first phases of the process – donation, procurement and testing – in order to ensure their quality and safety.

12. The proposal, however, excludes blood and blood products (other than blood precursors), human organs, as well as organs, tissues, or cells of animal origin. Blood

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[4] Data provided by Dr B. Loty of the Etablissement Français des Greffes.

and blood products currently are regulated by Directive 2001/83/EC[5], Directive 2000/70/EC[6] and Council Recommendation 98/463/EC[7], and a new directive based on public health principles is currently under discussion in Council and the European Parliament[8].

13. The transplantation of human organs requires a different policy approach due to their specific nature and the severe shortages that result in many patients going untreated. The Commission will address this subject shortly by inviting national and international organisations involved in organ procurement for an exchange of information on the relevant issues.

14. Organs, tissues, and cells of animal origin for human therapy are still in the research phase, but nevertheless pose different regulatory problems that will need to be addressed in due course.

15. Tissues and cells used as an autologous graft (tissues removed and transplanted back to the same person), within the same surgical procedure and without being subjected to any banking process, are also excluded from this proposal. The quality and safety considerations associated with this process are completely different.

16. Autologous cells used for medicinal products require a completely different regulatory approach and therefore are completely excluded from this Directive.

17. This Directive does not intend to cover research using human tissues and cells, such as when used for purposes other than application to the human body, i.e. in vitro research or in animal models. Only those cells and tissues that in clinical trials are applied to the human body should comply with the quality and safety standards laid down in this Directive.

18. All other types of tissues and cells are covered. Some, however, in particular germ cells, foetal cells/tissues and embryonic stem cells, pose particular ethical concerns. To date, there is no consensus among Member States upon which basic harmonised decisions at EU level can be taken with regards to their use or prohibition. If, however, a particular application of these cells is accepted in a Member State, the relevant provisions of this Directive will apply.

Processing, preservation, storage, and distribution of tissues and cells to be used for human transplantation

19. When the tissues and cells are to be used for human transplantation, this proposal for a Directive applies to the processing, preservation, storage, and distribution phases.

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5 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. OJ L 311, 28.11.2001, p.67-128.

6 Directive 2000/70/EC of the European Parliament and of the Council of 16 November 2000 amending Council Directive 93/42/EEC as regards medical devices incorporating stable derivates of human blood or human plasma. OJ L 313, 13.12.2000, p.22.

7 Council Recommendation of 29 June 1998 on the Suitability of blood and plasma donors and the screening of donated blood in the European Community. OJ No L 203, 21.07.1998, p.14

8 Proposal for a Directive of the European Parliament and of the Council setting standards of quality and safety for the collection, testing, processing, storage, and distribution of human blood and blood components and amending Council Directive 89/381/EEC. COM(2000)816 final. 13.12.2000. 2000/0323 (COD).

Transplantation aims to recover a lost tissue or cell function by transferring to the human body equivalent tissues or cells. If their preparation includes steps that influence growth or differentiation of these cells, additional safety measures might need to be considered in the future.

20. The proposal excludes these phases of the process, however, when the tissues or cells are to be used for other purposes such anti-tumoral vaccines or therapies where the objective is not to recover a function by transplanting equivalent cells or tissues. These new therapeutic approaches require different, and very specific, processing standards, which cannot be established now since the associated risks are still under investigation. Furthermore in those cases they will fall under the legislation covering medicinal products or medical devices.

21. The Scientific Committee on Medicinal Products and Medical Devices (SCMPMD) concluded[9] that the area of tissue engineering is not yet sufficiently developed, and clear boundaries cannot be drawn between it and other allied areas. Oversight for adequate control of the introduction and monitoring of tissue engineering processes in the European Union would require, in the opinion of the SCMPMD, specific legislation.

22. This proposal for a Directive, therefore, aims to ensure that tissues and cells used as source of these products should have the same level of quality and safety, compared with 'classical' transplantation. In this way, the Directive will help to facilitate indirectly their movement from one Member State to another. In addition, by establishing the same procurement, processing, and storage criteria, as well as the setting up of a Community register of accredited tissue banks, the Directive will help to remove uncalled-for restrictions on the exchange of tissues from one Member State to another.

Obligation of Member States authorities

23. This proposal does not interfere with decisions made by Member States concerning the use or non-use of any specific type of human cells, including germ cells and embryonic stem cells. If, however, any particular use of such cells is authorised in a Member State, this proposal will require the application of all provisions necessary to protect public health and guarantee respect for fundamental rights.

24. The therapeutic use of human tissues and cells involves a considerable number of complex and interrelated activities, extending from donor-suitability evaluation to the implantation of the graft, or the manufacturing of a product. Any prospective legislation must take all these steps into account, while respecting the responsibilities of the Member States for the organisation and delivery of health services and medical care.

25. This proposed Directive respects the different organisational structures established in Member States. In some, procurement is carried out only by tissue banks, while in others responsibility is shared by both procurement centres and the tissue banks. This proposal respects the authority of the Member States for granting accreditation to

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[9] 'Opinion on the state of the art concerning tissue engineering' adopted by the Scientific Committees on Medicinal Products and Medical Devices on 1st October 2001. Doc. SANCO/SCMPMD/2001/0006 Final

those establishments involved in tissue procurement while it sets out the high standards of quality and safety that must be met.

26. This proposed Directive seeks to ensure a high level of quality and safety throughout the 'tissue and cells transplantation chain' in all Member States, bearing in mind the freedom of movement of citizens and goods within the European Union. The establishment of quality and safety standards will help to reassure the public that human tissues and cells that are derived from donations in another Member State nonetheless carry the same guarantees as those in their own country.

27. In order to arrive at such standards, the proposed Directive requires the establishment of comparable national inspection and accreditation structures, as well as equivalent training for the personnel involved throughout the chain. The specific training provisions envisaged in this proposed Directive, however, are without prejudice to the legislative requirements concerning mutual recognition of diplomas.

28. Establishment of a system to ensure that all tissues and cells could be traced from donor to recipient and vice versa is an essential aim of this proposed Directive. It also establishes a system to monitor adverse reactions and events associated with the procurement, processing and use of tissues and cells in the European Union.

29. Importation of tissues and cells from third countries is on the increase. In order to protect the health of patients in the European Union, it is necessary to ensure that high standards of quality and safety are also applied to these imports. Due to the rapidity with which technology is evolving in this area, it will help Member States if appropriate EU procedures to ensure quality and safety for imports and exports of these human substances are developed. As a general principle, imports from and exports to from third countries should only be carried out by accredited tissue banks, supervised by the competent authority. Authorisation should be granted only if at least equivalent standards are met by the tissues and cells imported or exported. The Directive provides for a mechanism to establish an EU procedure that will allow a coherent approach to the authorisation of imports and exports.

Donor suitability and evaluation: quality, safety, and ethical concerns

30. Procurement, evaluation, and selection of the donor are the first and decisive steps in the transplantation chain. Donors are directly involved in these processes that are often conducted outside tissue banks. This proposed Directive will establish high standards of quality and safety for the processes associated with the selection and evaluation of the donor and procurement of the tissues and cells in order to ensure the health of recipients.

31. The use of human tissue and cells should take place under conditions protecting the rights and health of donors, potential donors, and recipients. This Directive protects their dignity and identity and established the principle that parts of the human body as such being used for tissue and cells procurement, or exchange and allocation activities should not give rise to financial gain.

32. It is generally accepted in all Member States that tissue and cell donation should be voluntary and unpaid. For germ cell donation, however, current practice does not always reflect this rule. The Commission considers that a Directive on tissues and

cells should endorse application of this ethical principle, which is cited in texts both of the Council of Europe and the European Group of Ethics.

33. Consent for procurement is in general regulated by Member States in very different ways. Their legislation ranges from 'presumed consent' to others regulations where consent of relatives is needed The Commission believes that in a field very much identified with ethical questions it would be inappropriate to attempt to resolve such issues under a Directive based on Article 152 which addresses public health issues. However, the procurement of human tissues and cells must fully respect the Charter of Fundamental Rights of the European Union, and take fully into account the principles of he Convention of Human Rights and Biomedicine. The Convention states that consent for living donors should be given expressly and freely, in writing prior to the donation. This Directive specifies that procurement human tissues or cells shall be carried out only after all mandatory consent requirements in force in the Member State are met.

Tissue banks

34. This proposed Directive reflects the importance of tissue banks, which have responsibility for the processing, preservation, internal quality control, storage, and distribution of the procured human tissues and cells, and must ensure the quality and safety during the entire process.

35. In 1994, the Council of Europe adopted Recommendation R 94/1[10], which addresses activities relating to the banking of human tissues (and cells). It recommends that: tissue banks should be officially licensed by national health administrations, or recognised by the competent authorities: that they should ensure that tissues are tested for transmissible diseases and stored safely; that records of all tissues retrieved and issued should be kept; that distribution should permit optimal use based on equal access; and that close co-operation should be ensured between all recognised exchange and tissue banking organisations. This Recommendation is fully taken into account in this proposal for a Directive.

36. Recommendation R 94/1 recommends that tissue procurement should be carried out on a not for profit basis-making, but in case of a public health need an authorised profit-making body may exist. This is in line with the opinion of the EGE, which expressed that: 'in principle, tissue bank activities should be reserved to public health institutions or non profit-making organisations. In such cases, this means that the delivery price should only cover the bank's expenses relating to the tissues in question. Nevertheless, given the current state of development of the sector, it is difficult to exclude tissue-banking activities by commercial organisations, such as large private laboratories. This is particularly true where human tissues are used as a basis for 'engineered' products requiring the use of sophisticated medical techniques. Tissue banks set up by industry, however, should be subject to the same licensing and monitoring requirements as non-commercial operators'. Taking into account these opinions, this proposal suggests that Member States shall encourage non-profit tissue banks, without introducing a strict legal obligation.

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10 Council of Europe. Recommendation No R (94) 1 of the Committee of Ministers to Member States on Human tissue banks. Adopted by the Committee of Ministers on 14 March 1994, at the 509th meeting of the Ministers' Deputies).

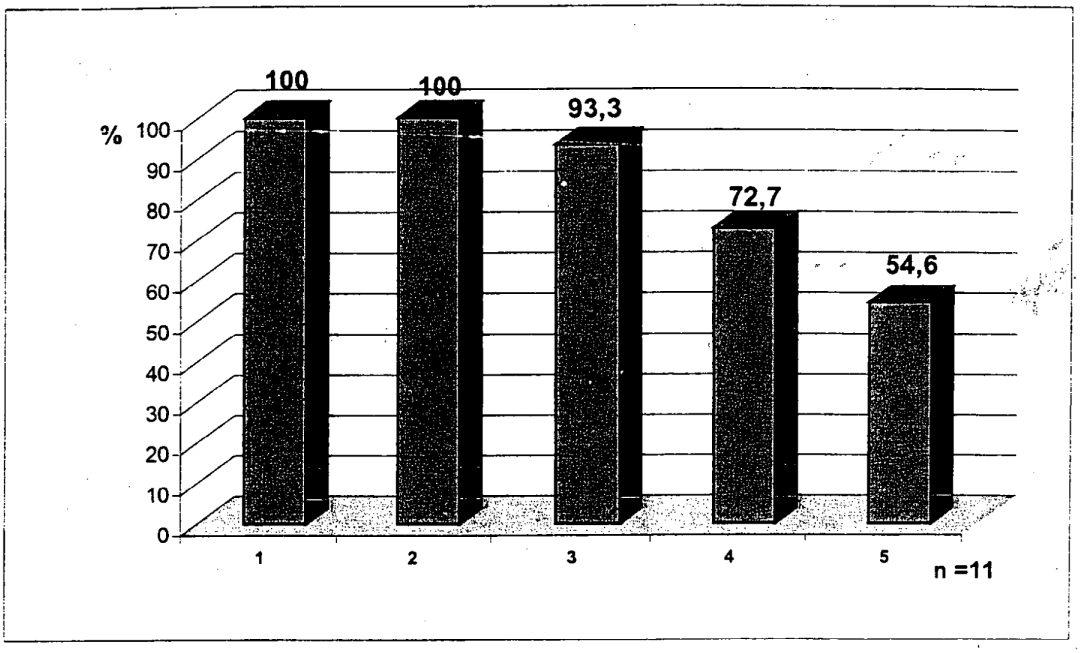
37. The proposal contains measures to ensure that technical requirements and standards keep pace with scientific progress. To this end, a new Regulatory Committee of Member State representatives is established. This procedure will be used for regularly updating the technical annexes of this Directive, in particular in view of technical and scientific progress, and emerging risks of transmission of communicable diseases. In the preparation of regularly updated standards, the Commission intends to collaborate closely with the Council of Europe, the World Health Organisation, and other relevant international bodies.

38. EUROPEAN UNION PROVISIONS OF RELEVANCE TO TISSUES AND CELLS

Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. (OJ L 311, 28.11.2001, p. 67-128)
Directive 2000/70/EC of the European Parliament and of the Council of 16 November 2000 amending Council Directive 93/42/EEC as regards medical devices incorporating stable derivates of human blood or human plasma. (OJ L 313, 13.12.2000, p.22.)
Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices. (OJ L 331, 7.12.1998, p.1)
Council Directive of 93/42/EEC of 14 June 1993 concerning medical devices. (OJ L 169, 12.07.1993)
Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products. (OJ L 214, 24.08.1993, p.1)
Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable medical devices (OJ L 189, 20.07, 1990, p.17)
Council Decision 87/67/EEC of 26 January 1987 accepting on behalf of the Community the European agreement on the Exchange of Therapeutic Substances of Human Origin. (OJ L 37, 7.02.1987, p.1)
Commission Regulation (EC) No 540/95 of 10 March 1995 laying down the arrangements for reporting suspected unexpected adverse reactions which are not serious, whether arising in the Community or in a third country, to medicinal products for human or veterinary use authorised in accordance with the provisions of Council Regulation (EEC) No 2309/93. (OJ L 55, 11.03.1995, p.5)

TABLE 1

Protection of the donor.
Percentage of reporting Member States (n=11) that have mandatory requirements

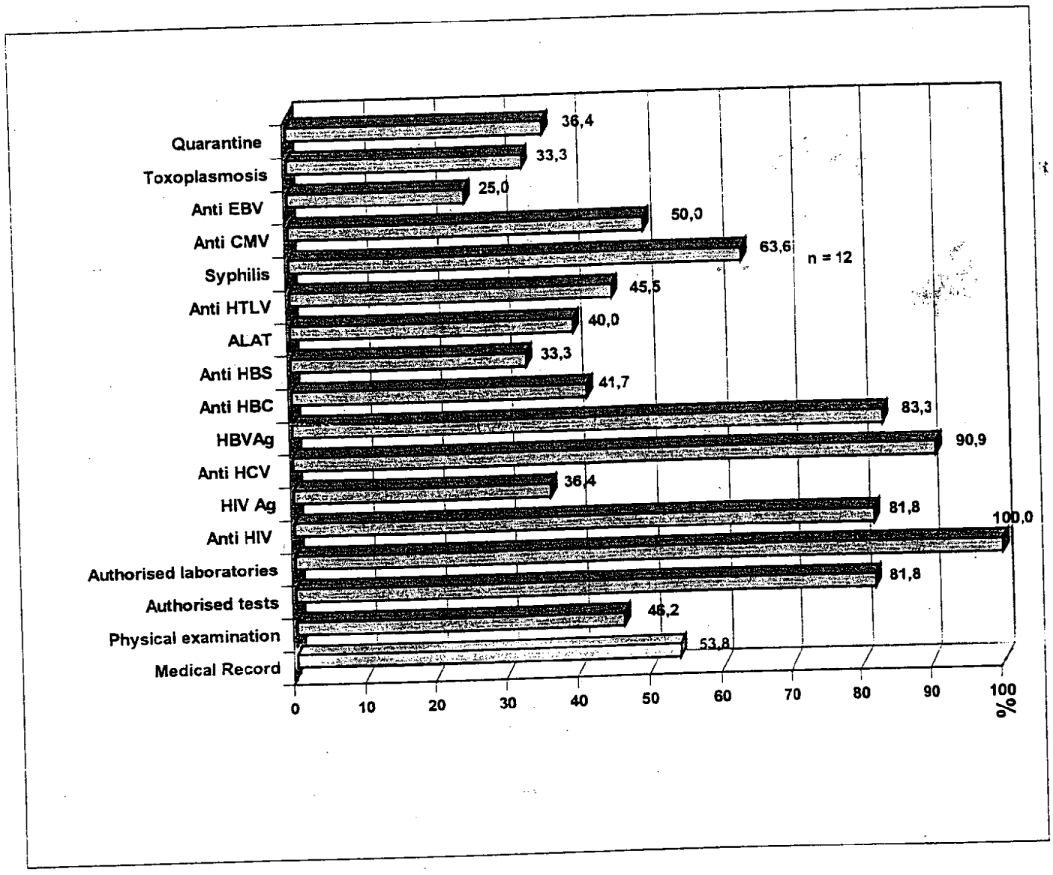


1. Voluntary and non-remunerated donations
2. Respect for the anonymity of donor / recipient.
3. Specific rules for expressions of consent for living donors.
4. Specific rules for minors.
5. Family consent required for deceased donor.

TABLE 2

Suitability of the donor.

Percentage of reporting Member States (n=12) that have mandatory requirements

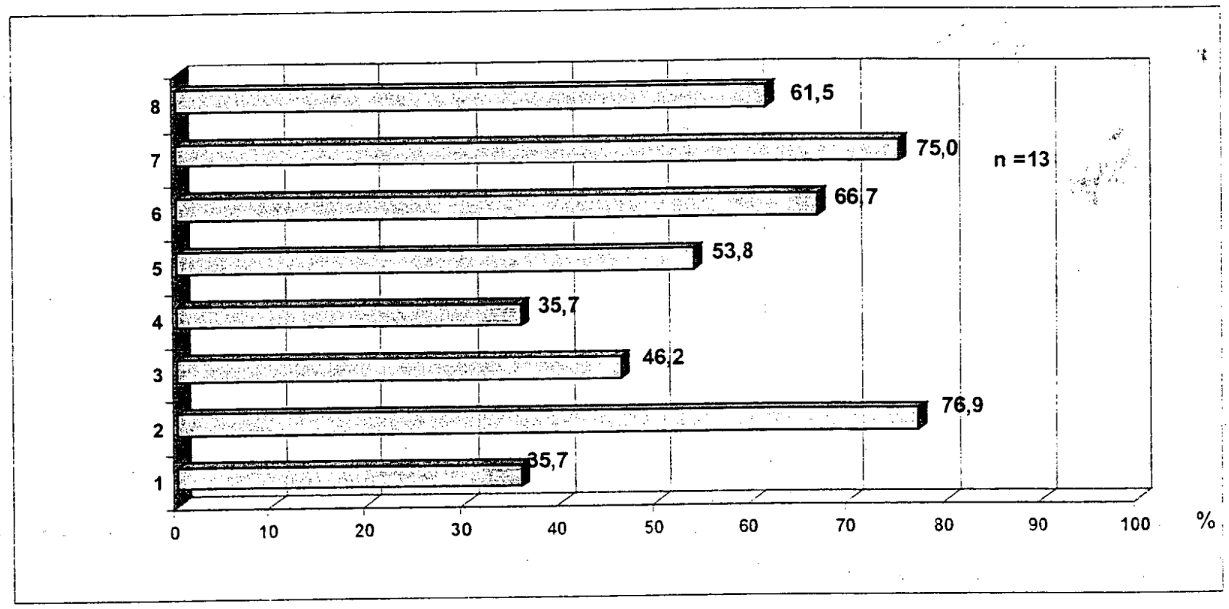


Quarantine – Quarantine for living donor; **Toxoplasmosis** – Test for the detection of toxoplasmosis; **Anti EBV** – Epstein Bar Virus antibodies; **Anti CMV** – Cytomegalovirus antibodies; **Syphilis** – Treponema Pallidum; **Anti HTLV** – Human T Lymphotrophic virus antibodies; **ALAT** – Alanin Aminotransferase enzyme; **Anti HBS** – Hepatitis B virus antibodies (surface); **Anti HBC** – Hepatitis B virus antibodies (core); **HBV Ag** – Hepatitis B virus Antigen; **Anti HCV** – Hepatitis C virus antibodies; **HIV Ag** – Human Immunodeficiency Antigen; **Anti HIV** – Human Immunodeficiency virus antibodies; Use of authorised laboratories; Use of authorised test; Requirement for physical examination; Consultation of medical records.

TABLE 3

Other regulatory aspects.

Percentage of reporting Member States (n=13) that have mandatory requirements



1. Required authorisation for procurement establishments.
2. Required authorisation for processing organisations.
3. Standards for processing.
4. Standards for transport.
5. Standards for retrieval.
6. Required inspection.
7. Authorisation for import / export.
8. Reporting adverse events.

JUSTIFICATION

A. AIMS

The aims of this proposal are to:

- establish European Community legislation setting standards for the quality and safety of tissues and cells of human origin used for application in the human body;
- strengthen requirements related to the suitability of donors of tissues and cells and the screening of donated substances of human origin in the European Union;
- establish at Member State level requirements for establishments involved in the procurement, testing, processing, storage, and distribution of tissues and cells of human origin, as well as national accreditation and monitoring structures;
- lay down provisions at Community level for the formulation of a register of accredited establishments;
- lay down provisions at Community level for the formulation of a quality system for tissues and cells related establishments;
- lay down common provisions at Community level for the training of staff directly involved in the procurement, testing, processing, storage, and distribution of tissues and cells of human origin, without prejudice to existing legislation;
- establish rules for ensuring the traceability of tissues and cells of human origin from donor to patient and vice versa, which are valid throughout the European Union;
- establish a system for the regulation of imports of human tissues and cells from third countries that ensure equivalent standards of quality and safety.

B. LEGAL BASIS

The legal basis for this proposal is Article 152 of the Treaty, in particular (4)(a), which requires the European Parliament and the Council to adopt measures that set high standards of quality and safety of substances of human origin.

C. SUBSIDIARITY AND PROPORTIONALITY

In accordance with the principles of subsidiarity and proportionality, European Community actions in the public health field should be undertaken only if their objective cannot be sufficiently achieved by the Member States and can therefore, by reason of their scale and effects, be better achieved by the EC. This is reinforced in Article 152 which states that Community public health action shall fully respect the

responsibilities of the Member States for the organisation and delivery of health services and medical care.

Article 152, however, goes on to specify in (4)(a) that measures should be adopted setting high standards of quality and safety of organs and substances of human origin, blood and blood derivatives. In the light of this, actions should address issues that have a trans-national dimension, where common approaches are required, or where there is a need for effective co-operation and co-ordination.

The measures set out in this proposed Directive incorporate requirements for the procurement, testing, processing, storage, and distribution of tissues and cells of human origin intended for application in the human body. They do not prevent Member States from maintaining or introducing more stringent protective measures, in conformity with the Treaty, and do not affect national provisions on the donation or medical use of tissues and cells of human origin.

In contrast to existing European Community procedures concerning the approximation of laws, regulations and administrative provisions relating to proprietary medicinal products, this proposed Directive does not have as its primary objective the placing on the market of tissues and cells of human origin. It will, however, mean that national provisions resulting from the transposition of this proposed Directive will result in homogeneity of technical requirements of quality and safety within the Member States once it has been adopted.

This proposed Directive, in particular, establishes an equivalent system of notification and accreditation for establishments involved in the procurement, testing, processing, storage, and distribution of tissues and cells of human origin in the Member States. Although criteria for this system are laid down in this proposed Directive, detailed rules remain the responsibility of the Member States.

D. LEGISLATIVE AND ADMINISTRATIVE SIMPLIFICATION

The impact of this proposed Directive, once adopted and transposed in the Member States, will establish a minimum regulatory and administrative foundation that will facilitate the exchange of tissues and cells of human origin in the European Union.

In ensuring an equivalent collection of data on any incidents arising during the donation, procurement, testing, processing, storage, and distribution of tissues and cells of human origin, this proposed Directive will simplify the exchange of information in this field between the Member States.

E. CONSISTENCY WITH OTHER COMMUNITY POLICIES

This proposed Directive is complementary to European Community legislation relating to the quality and safety of human blood and blood components. It is intended to ensure the same level of quality and safety of tissues and cells used for application in the human body.

F. OUTSIDE CONSULTATION

This proposal for a Directive takes account of the most recent progress made and agreements attained at international level, particularly within the World Health Organisation and the Council of Europe.

In addition, there have been a number of consultations with competent technical experts and with representatives of the Member States in its preparation. Most of the organisations interested in the field have been consulted, such the European Association of Tissue Banks, the European Association of Musculoeskeletal Transplantation, the European Eye Bank Association, the European Group for Bone Marrow Transplantation, the Donor Bone Marrow Association, Europdonor Foundation, representatives of the industry and patients associations.

Provisions in order to ensure a high level of quality and safety for the processing, preservation, storage, and distribution of human tissues and cells are set up in Articles 16 to 25 referring to the technical annexes. In these provisions, staff training and the adoption of a quality control system to be established in these health care establishments are envisaged.

As a contribution to ensuring safety and quality throughout the tissues and cells transplantation process, an information exchange system needs to be established between Member States. To be effective, this system has to rely on traceability of tissues and cells of human origin throughout the transplantation process, using suitable labelling as well as using a system of conservation of the files. This labelling and the adoption of provisions concerning the maintenance of the files foreseen in Articles 7, 13 and 26, will facilitate any action that may need to be taken 'upstream' in the 'chain' in the event of 'downstream' incidents and will highlight any event occurring, after donation, in the transplantation chain.

Lastly, in view of rapid scientific developments related to the safety and quality of tissues and cells of human origin, continual and rapid adaptation of the proposal's annexes to technical progress has to be foreseen. A committee procedure is envisaged in Article 28 to address this. Such adaptations will be carried out on a solid scientific basis. The Commission intends to collaborate closely with the Council of Europe when these adaptations are developed, in order to ensure coherence with the recommendations it develops in the same field.

2002/0128(COD)

Proposal for a

DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on setting standards of quality and safety for the donation, procurement, testing, processing, storage, and distribution of human tissues and cells

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 152(4)(a) thereof,

Having regard to the proposal from the Commission[1],

Having regard to the Opinion of the Economic and Social Committee[2],

Having regard to the Opinion of the Committee of the Regions[3],

Acting in accordance with the procedure laid down in Article 251 of the Treaty[4],

Whereas:

(1) The extensive therapeutic use of human tissues and cells for application in the human body demands that their quality and safety be ensured in order to prevent the transmission of diseases.

(2) The availability of tissues and cells of human origin used for therapeutic purposes is dependent on Community citizens who are prepared to donate them. In order to safeguard public health and to prevent the transmission of infectious diseases by these tissues and cells, all precautionary measures need to be taken during their procurement, processing, storage, distribution and use.

(3) There is an urgent need for a unified framework in order to ensure high standards of quality and safety with respect to the procurement, testing, processing, storage and distribution of tissues and cells across the Community and to facilitate exchanges for the thousand of patients receiving this type of therapy each year. It is essential, therefore, that whatever their intended use, Community provisions should ensure that tissues and cells of human origin are of comparable quality and safety. The establishment of such standards, therefore, will help to reassure the public that human tissues and cells that are procured in another Member State, nonetheless, carry the same guarantees as those in their own country.

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1 OJ C [...], [...], p. [...].
2 OJ C [...], [...], p. [...].
3 OJ C [...], [...], p. [...].
4 OJ C [...], [...], p. [...].

(4) It is necessary to regulate the donation, procurement, and testing of all sources of human tissues and cells intended for application in the human body.. The processing, preservation, storage and distribution of all human tissues and cells used for transplantation purposes should also be regulated. However, cells for autologous use should be excluded from the scope if they are to be used for the manufacturing of medicinal products. Tissues and allogeneic cells intended to be used for industrially manufactured products, including medical devices, should be covered only as far as donation, procurement and testing are concerned. The further manufacturing steps are covered by the relevant legislation[5].

(5) The proposal excludes blood and blood products (other than haematopoietic progenitor cells), human organs, as well as organs, tissues, or cells of animal origin. Blood and blood products currently are regulated by Directive 2001/83/EC[5], Directive 2000/70/EC[6] and Council Recommendation 98/463/EC[7], and a new directive based on public health principles is currently under discussion in Council and the European Parliament[8]. Tissues and cells used as an autologous graft (tissues removed and transplanted back to the same person), within the same surgical procedure and without being subjected to any banking process, are also excluded from this proposal. The quality and safety considerations associated with this process are completely different.

(6) This Directive does not cover research using human tissues and cells, such as when used for purposes other than application to the human body, i.e. in vitro research or in animal models. Only those cells and tissues that in clinical trials are applied to the human body should comply with the quality and safety standards laid down in this Directive.

(7) This Directive does not interfere with decisions made by Member States concerning the use or non-use of any specific type of human cells, including germ cells and embryonic stem cells. If, however, any particular use of such cells is authorised in a Member State, this Directive will require the application of all provisions necessary to protect public health and guarantee respect for fundamental rights. Moreover, this Directive does not interfere with provisions of Member States defining the legal term 'person' or 'individual'.

(8) The donation, procurement, processing, preservation, storage and distribution of human tissues and cells for transplantation should comply with high standards of quality and safety in order to ensure a high level of health protection in the Community. This Directive should establish standards for each one of the steps in the human tissues and cells transplantation process.

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5 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. OJ L 311, 28.11.2001, p.67-128.

6 Directive 2000/70/EC of the European Parliament and of the Council of 16 November 2000 amending Council Directive 93/42/EEC as regards medical devices incorporating stable derivates of human blood or human plasma. OJ L 313, 13.12.2000, p.22.

7 Council Recommendation of 29 June 1998 on the Suitability of blood and plasma donors and the screening of donated blood in the European Community. OJ No L 203, 21.07.1998, p.14

8 Proposal for a Directive of the European Parliament and of the Council setting standards of quality and safety for the collection, testing, processing, storage, and distribution of human blood and blood components and amending Council Directive 89/381/EEC. COM(2000)816 final. 13.12.2000. 2000/0323 (COD)

(9) It is necessary to increase confidence among the Member States in the quality and safety of donated tissues and cells, in the health protection of living donors and respect for deceased donors, and in the safety of the transplantation process.

(10) Tissues and cells used for allogeneic therapeutic purposes can be procured from both living and deceased donors. In order to ensure that the health status of a living donor is not affected by the donation, a prior medical examination is required. The dignity of the deceased donor has to be respected.

(11) The use of tissues and cells for application in the human body can cause diseases and unwanted effects. Most of these can be prevented by careful donor evaluation and the testing of each donation in accordance with rules established and updated according to the best available scientific advice.

(12) As a matter of principle, tissue and cell transplantation programmes should be founded on the philosophy of voluntary and unpaid donation, anonymity of both donor and recipient, benevolence of the donor and encouragement of the absence of profit by establishments involved in tissue and cell transplantation services.

(13) The procurement of human tissues and cells must fully respect the Charter of Fundamental Rights of the European Union[9], and take fully into account the principles of the Convention on Human Rights and Biomedicine of the Council of Europe[10], in particular in relation to donor consent.

(14) All necessary measures need to be taken in order to provide prospective donors of tissues and cells with assurances regarding the confidentiality of any health related information provided to the authorised personnel, the results of tests on their donations, as well as any future traceability of their donation.

(15) Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and the free movement of such data [11], applies to personal data processed in application of the present directive. Article 8 of this Directive prohibits in principle the processing of data concerning health. Limited exemptions to this prohibition principle are foreseen. Directive 95/46/EC provides also that the controller must implement appropriate technical and organisational measures to protect personal data against accidental or unlawful destruction or accidental loss, alteration, unauthorised disclosure or access and against all other unlawful forms of processing.

(16) An accreditation system for tissue banks and a system for notification of adverse events and reactions linked to the procurement, processing, testing, storage, and distribution of tissues and cells of human origin should be established in Member States.

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9 OJ C 364, 18.12.2000, p.1.

10 Council of Europe. Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on human rights and biomedicine. *European Treaty Series - No. 164.* Oviedo, 4.IV.1997. p.11

11 OJ L 281, 23.11.1995, p.31.

(17) Member States should organise inspection and control measures, to be carried out by officials representing the competent authority, to ensure compliance of the tissue establishments with the provisions of this Directive.

(18) Personnel directly involved in the donation, procurement, testing, processing, preservation, storage and distribution of tissues and cells of human origin should be appropriately qualified and provided with timely and relevant training The provisions laid down in this Directive as regards training should be applicable without prejudice to existing Community legislation on the recognition of professional qualifications.

(19) An adequate system to ensure the traceability of tissues and cells of human origin should be established; traceability should be enforced through accurate substance, donor, recipient, tissue bank, and laboratory identification procedures as well as record maintenance and an appropriate labelling system.

(20) In order to increase the effective implementation of the provisions adopted under this Directive, it is appropriate to provide for penalties to be applied by Member States.

(21) Since the objectives of the proposed action, namely to set high standards of quality and safety for human tissues and cells throughout the Community cannot be sufficiently achieved by the Member States alone and can therefore, by reason of scale and effects, be better achieved at Community level, the Community may adopt measures in accordance with the principles of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality, as set out in that Article, this Directive does not go beyond what is necessary for this purpose.

(22) It is necessary that the best possible scientific advice is available to the Community in relation to the safety of tissues and cells; in particular in order to assist the Commission in adapting the provisions of this Directive to scientific and technical progress.

(23) The opinions of the Scientific Committee for Medicinal Products and Medical Devices and that of the European Group on Ethics in Science and New Technologies, have been taken into account as well as international experience in this field, and will be sought in the future whenever necessary.

(24) Since the measures necessary for the implementation of this Directive are measures of general scope within the meaning of Article 2 of Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission [12], they should be adopted by use of the Regulatory Procedure provided for in Article 5 of that Decision.

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12 OJ L 184, 17.7.1999, p.23.

HAVE ADOPTED THIS DIRECTIVE:

CHAPTER I

GENERAL PROVISIONS

Article 1

Objective

This Directive lays down standards of quality and safety of human tissues and cells used for application to the human body, in order to ensure a high level of protection of human health

Article 2

Scope

1. The provisions of this Directive shall apply to the donation, procurement, and testing of human tissues and cells for application to the human body. The provisions of this Directive shall also apply to the processing, preservation, storage and distribution of human tissues and cells when they are to be used for human transplantation.

   In the case of industrially manufactured products derived from tissues and cells, this Directive applies only to donation, procurement and testing.

2. This Directive does not apply to:

   a) tissues and cells used as an autologous graft within the same surgical procedure;

   b) autologous cells to be used for the manufacturing of medicinal products;

   c) blood and blood components as defined by [Directive of the European Parliament and of the Council setting standards of quality and safety for the collection, testing, processing, storage, and distribution of human blood and blood components and amending Council Directive 89/381/EEC.];

   d) organs.

Article 3

Definitions

For the purposes of this Directive:

a) '*Cells*' shall mean individual cells or a collection of cells when not bound by any form of connective tissue.

b) '*Tissue*' shall mean all constituent parts of the human body formed by cells.

c) '*Donor*' shall mean a living or deceased individual, including *non-natus,* who is the source of cells or tissues.

d) '*Organ*' shall mean 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.

e) '*Procurement*' shall mean a process by which the donated tissue or cells become available.

f) '*Processing*' shall mean all operations involved in the preparation, manipulation, preservation and packaging of tissues or cells for transplantation.

g) '*Preservation*' shall mean the use of chemical agents, alterations in environmental conditions or other means during processing to prevent or retard biological or physical deterioration of cells or tissues.

h) '*Quarantine*' shall mean the status of retrieved tissue or cells or packaging material, or tissue isolated physically or by other effective means whilst awaiting a decision on their release or rejection.

i) '*Distribution*' shall mean transportation and delivery of tissues or cells for storage, processing or use in recipients.

j) '*Transplantation*' shall mean the process of reconstituting a function by transferring equivalent cells and/or tissues to a recipient.

k) '*Serious adverse event*' shall mean any untoward occurrence associated with the procurement, testing, processing, storage and distribution of 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.

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

m) '*Tissue bank*' shall mean the establishment, public or private, that is responsible for the activities of processing, preservation, storage, and distribution of tissue and cells. It may also be responsible for the procurement of tissues and cells.

n) '*Tissue establishment*' shall mean a tissue bank or health care establishment that hosts a tissue procurement team.

o) '*Tissue procurement team*' shall mean the health care professionals involved in any of the activities necessary for tissue and cell procurement.

p) '*Allogeneic use*' shall mean cells or tissues transplanted from one person to another.

q) '*Autologous use*' shall mean cells or tissues removed from and transplanted back to the same person.

Article 4

Implementation

1. Member States shall designate the competent authority or authorities responsible for implementing the requirements of this Directive.

2. This Directive shall not prevent a Member State from maintaining or introducing more stringent protective measures that comply with the provisions of the Treaty.

3. In carrying out the activities covered by this Directive, the Commission may have recourse to technical and/or administrative assistance to the mutual benefit of the Commission and of the beneficiaries, relating to identification, preparation, management, monitoring, audit and control, as well as to support expenditure.

CHAPTER II

OBLIGATIONS ON MEMBER STATES AUTHORITIES

Article 5

Supervision of tissue procurement

1. Member States shall take all necessary measures to ensure that tissue procurement teams are either part of a tissue bank or a health care establishment duly accredited and inspected

2. Member States shall take all necessary measures to ensure that tissue procurement teams are notified to the competent authority and that the procurement, including the staff involved, complies with the requirements listed in Part A of Annex I.

Article 6

Accreditation of tissue banks

1. Member States shall ensure that all activities relating to the processing, preservation, storage, and distribution of human tissues and cells for human transplantation are undertaken only by tissue banks that have been accredited by a competent authority for that purpose.

2. Haematopoietic progenitor cells from peripheral blood, umbilical cord and bone marrow, however, may be distributed directly from the health care establishment

where the procurement is carried out, which could not be accredited as a tissue bank, to a health care establishment for immediate transplantation.

3. The competent authority, having verified that the tissue bank complies with the requirements set out in Annex I, shall accredit the tissue bank and indicate which activities it may undertake and which conditions apply.

4. The tissue bank shall not undertake any substantial changes to its activities without the prior written approval of the competent authority.

5. The competent authority may suspend or revoke the accreditation of a tissue bank if inspection or control measures demonstrate that it does not comply with the requirements of this Directive.

Article 7

Register of accredited tissue banks and reporting obligations

1. The competent authority shall establish and maintain a publicly accessible register of tissue banks specifying the activities for which they have been accredited.

2. Tissue banks shall maintain an official record on the origin and destination of the tissues and cells processed for application in the human body. An annual report of these activities shall be submitted to the competent authority.

3. Member States and the Commission shall establish a network of the national tissue bank registers.

Article 8

Inspection and control measures

1. Member States shall ensure that the competent authority organises inspections and that tissue banks carry out appropriate control measures in order to ensure that the requirements of this Directive are complied with.

2. The competent authority shall also organise inspections and ensure that appropriate control measures are in place in health care establishments where the procurement of human tissues and cells is carried out, as well as in establishments of third parties as specified in Article 24.

3. Inspections and control measures shall be organised by the competent authority on a regular basis. The interval between two inspections and control measures shall not exceed two years.

4. Inspections and control measures shall be carried out by officials representing the competent authority who must be empowered to:

   a) inspect health care establishments involved in procurement, accredited tissue banks, as well as the facilities of any third parties;

b) evaluate the procedures and the activities carried out by the health care establishments, tissue banks and the facilities of third parties;

c) examine any documents relating to the subject of the inspection.

5. The competent authority shall organise inspections and other control measures as appropriate in the event of any serious adverse reaction or serious adverse event.

6. Member States shall, upon the request of another Member State or the Commission, provide information about the results of inspections and control measures carried out in individual tissue banks, healthcare establishment or the facilities of third parties.

Article 9

Import/Export of human tissues and cells

1. Member States shall take all necessary measures to ensure that all imports of human tissues or cells from third countries are approved by the competent authority. All tissues and cells that are exported to third countries shall comply with the requirements of this Directive.

2. The import/export of human tissues and cells for transplantation shall be undertaken only through accredited tissue banks.

3. The competent authority shall approve imports of human tissues and cells from third countries only when equivalent standards of quality and safety to the ones laid down in this Directive are ensured.

4. The procedures for verifying the equivalent standards of quality and safety in accordance with paragraph 3 shall be established by the Commission in accordance with the procedure referred to in Article 30(2).

Article 10

Traceability

1. Member States shall ensure that tissue establishments take all necessary measures to ensure that all tissues and cells procured, processed, stored and distributed on their territory can be traced from the donor to recipient and vice versa.

2. The procedures for ensuring traceability at the Community level shall be established by the Commission according to the procedure referred to in Article 30(2)

3. Tissue establishments shall implement a donor identification system and assign a code to each donation and its products.

4. All tissues and cells must be identified with a label that contains the information listed in Annexes VI and VII.

Article 11

Notification of serious adverse events and reactions

1. The Member States shall ensure that there is a system in place to report, register, and transmit information about serious adverse events and reactions related to the procurement, testing, processing, storage, distribution and transplantation of tissues and cells.

2. The responsible person referred to in Article 17 shall notify the competent authority of any serious adverse events and reactions referred to in paragraph 1 and provide a report analysing the cause and the ensuing outcome.

3. The procedure for notifying adverse events and reactions shall be established by the Commission in accordance with the procedure referred to in Article 30(2).

CHAPTER III

DONOR SELECTION AND EVALUATION

Article 12

Principles for tissue and cell donation

1. Member States shall encourage voluntary and unpaid donations of tissues and cells with a view to ensuring that they are in so far as possible provided from such donations

2. Member States shall take all necessary measures to ensure that any promotion and publicity activities in support of the donation of human tissues and cells receive prior approval by the competent authority. Advertising the need for, or availability of, human tissues and cells, with a view to offering or seeking financial gain or comparable advantage shall be prohibited.

3. Member States shall encourage that the procurement of tissues and cells is carried out on a non-profit basis.

Article 13

Consent

1. The procurement of human tissues or cells shall be carried out only after all mandatory consent requirements in force in the Member State are met.

2. Member States shall take all necessary measures to ensure that the recipients, donors or their families are provided with the information listed in Annex III.

Article 14

Data protection and confidentiality

1. Member States shall take all necessary measures to ensure that all data, including genetic information, collated within the scope of this Directive and to which third parties have access have been rendered anonymous so that the donor and the recipient are no longer identifiable.

2. For that purpose, they shall ensure that:

   a) data security measures are in place as well as safeguards against any unauthorised data additions, deletions, or modifications to donor files or deferral records, as well as any transfer of information;

   b) procedures are in place to resolve data discrepancies; and

   c) no unauthorised disclosure of information occurs, whilst guaranteeing the traceability of donations.

3. Member States shall take all necessary measures to ensure that the identity of the recipient(s) is not disclosed to the donor or his family and vice versa, without prejudice to legislation in force in Members States on the conditions of disclosure if the donor is closely related to the recipient.

Article 15

Selection, evaluation, and procurement

1. The tissue procurement team shall ensure that the donor evaluation and selection is carried out according to the requirements specified in Annex IV.

2. The tissue procurement team shall ensure that tissues and cells are procured, packaged and transported to the tissue banks in accordance with Annex VI.

3. In the case of an autologous donation, the suitability criteria shall be established and documented by the physician responsible for the patient, according to the clinical record, the therapeutic indication, and in accordance with the requirements listed in point 2.1 of Annex IV.

4. The tissue banks shall ensure that the selection and acceptance of tissues and cells comply with the requirements of Annex VI. They shall also ensure that all donations are tested in accordance with Annex V.

5. The results of the donor evaluation and testing procedures shall be documented and any relevant abnormal findings shall be reported in accordance with Annex III.

6. The competent authority shall ensure that all the activities related to tissue procurement shall be carried out in accordance with the conditions specified in Annex VI.

CHAPTER IV

PROVISIONS FOR QUALITY AND SAFETY IN TISSUE PROCESSING

Article 16

Quality management

1. Member States shall take all necessary measures to ensure that each tissue establishment sets up and maintains a quality management system.

2. The Commission shall establish in accordance with the procedure laid down in Art 30(2) the Community standards and specifications, referred to in Annex II, for the activities relating to a quality management system.

3. Tissue establishments shall take all necessary measures in order to ensure that the quality management system includes at least the following documentation:

   - Standard Operating Procedures;
   - Guidelines;
   - Training and reference manuals;
   - Reporting forms;
   - Donor records.

4. Tissue establishments shall take all necessary measures to ensure that this documentation is available for official inspections.

5. Tissue establishments shall keep donor records for a minimum of 30 years after the confirmed clinical use of the last tissue/cell.

Article 17

Responsible person

1. Tissue banks shall designate a responsible person. This person shall fulfil the following minimum conditions and qualifications:

   a) he / she shall 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;

   b) he / she shall have at least two years practical experience, in one or more tissue banks accredited in accordance with Article 6.

2. The designated person referred to in paragraph 1 shall be responsible for:

a) ensuring that every unit of tissues and cells of human origin has been procured and tested for application in the human body and processed, stored, and distributed, when intended for transplantation, in compliance with the laws in force in the Member State;

b) providing information to the competent authority as required in Article 6;

c) implementing the requirements of Articles 7, 10, 11, 15, 16, and 18 to 25 in the tissue bank.

3. Tissue banks shall notify the competent authority of the name of the responsible person referred to in paragraph 1. Where the responsible person is permanently or temporarily replaced, the tissue bank shall provide immediately to the competent authority the name of the new responsible person and his or her date of commencement.

Article 18

Personnel

Personnel directly involved in activities related to the procurement, processing, preservation, storage and distribution of tissues and cells in a tissue establishment shall be qualified to perform such tasks and shall be provided with the relevant training specified in Annex II.

Article 19

Tissue and cell reception

1. The tissue bank shall ensure that human tissue and cells and associated documentation comply with the requirements listed in Annex VI. The documentation to be verified for each tissue or cell is listed in Parts D and E of Annex VI.

2. The tissue bank shall ensure and record the fact that the packaging conditions of the human tissue and cells received comply with the provisions listed in Annex VI. Any tissues and cells that do not comply with these provisions should be discarded in accordance with Annex VI.

3. The acceptance or rejection of the incoming tissues/cells shall be documented.

4. Tissue banks shall ensure that human tissues and cells are correctly identified at all times. Each delivery or batch of tissues or cells must be assigned an identifying code, in accordance with Article 10.

Article 20

Tissue and cell processing

1. The tissue bank shall include in its Standard Operating Procedures all the processing that directly affect quality and safety, and shall ensure that they are carried out under controlled conditions. The tissue bank shall ensure that the equipment used, the

working environment, process design, validation, and control conditions are in compliance with Annex VII.

2. Any modifications to the processes used in the preparation of the tissues and cells shall also meet the criteria laid down in paragraph 1.

3. The tissue bank must make special provisions in its Standard Operating Procedures for the handling of tissues and cells to be discarded in order to prevent the contamination of other tissues or cells, the processing environment, or personnel.

Article 21

Tissue and cell storage conditions

1. Tissue banks shall ensure that all procedures associated with the storage of tissues and cells are documented in the Standard Operating Procedures and that the storage conditions comply with requirements listed in Annex VII.

2. Tissue banks shall ensure that all storage processes are carried out under controlled conditions.

3. Tissue banks shall establish and maintain procedures for the control of packaging and storage areas, in order to prevent any condition that might adversely affect the function or integrity of tissue and cells.

4. Processed tissues or cells must be held in quarantine until released by the responsible person referred to in Article 17. Tissues or cells must not be released from quarantine for preservation and storage until all the requirements laid down in the Standard Operating Procedures have been met.

Article 22

Labelling, user information and packaging

Tissue banks shall ensure that labelling, documentation, and packaging conform to the requirements listed in Annex VII Parts D and E.

Article 23

Transport and distribution

The tissue bank shall guarantee the quality of tissues or cells until delivery. Distribution conditions shall comply with the requirements listed in Annex VII.

Article 24

Relationship of tissue banks with third parties

1. A tissue bank shall establish a written agreement with a third party in the following circumstances:

a) where a third party take responsibility in one phase of tissue or cell processing on behalf of the tissue bank;

b) where a third party provides goods and services that affect tissue or cell quality and safety assurance;

c) where a tissue bank provide services to another tissue bank;

d) where a tissue bank distributes tissue or cells processed by third parties.

2. The tissue bank shall evaluate and select third parties on the basis of their ability to meet the standards laid down in this Directive.

3. Tissue banks shall notify to the competent authority the complete list of agreements that they have established with third parties.

4. The agreements between tissue bank and third parties shall specify responsibilities to be carried out by the third party and detailed procedures.

5. Tissue banks shall provide copies of agreements with third parties when required by the competent authority.

Article 25

Access to human tissues and cells

1. Member States shall ensure that public and private establishments involved in health care, and establishments authorised to manufacture medicinal products or medical devices, have access to human tissue and cells, without prejudice to the provisions in force in Member States on the use of certain tissues and cells.

2. Such establishments shall report relevant information to the tissue banks in order to facilitate traceability, and ensure quality control and safety.

CHAPTER V

EXCHANGE OF INFORMATION, REPORTS, AND PENALTIES

Article 26

Coding of information

1. Member States shall establish a system for the identification of human tissues and cells, in order to ensure the traceability of all human tissues and cells, as indicated in Article 10.

2. The Commission, in co-operation with Member States, shall design a single European coding system that will provide the basic description and properties of tissues and cells.

Article 27

Reports

1. Member States shall send the Commission, three years after the implementation date indicated in Article32 (1), and every three years thereafter, a report on the activities undertaken in relation to the provisions of this Directive, including an account of the measures taken in relation to inspection and control.

2. The Commission shall transmit to the European Parliament, the Council, the Economic and Social Committee, and the Committee of the Regions, the reports submitted by the Member States on the experience gained in implementing this Directive.

Article 28

Penalties

Member States shall lay down the rules on penalties applicable to infringements of the national provisions adopted pursuant to this Directive and shall take all measures necessary to ensure that they are implemented. The penalties provided for must be effective, proportionate, and dissuasive. Member States shall notify those provisions to the Commission by the date specified in Article 33(1) at the latest and shall notify it without delay of any subsequent amendments affecting them.

CHAPTER VI

CONSULTATION OF COMMITTEES

Article 29

Adaptation to technical and scientific progress

The adaptation of the technical requirements set out in Annexes I to VII to technical and scientific progress shall be decided by the Commission in accordance with the procedure referred to in Article 30(2).

Article 30

Regulatory procedure

1. The Commission shall be assisted by a Committee, composed of representatives of the Member States and chaired by the representative of the Commission.

2. Where reference is made to this paragraph, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

3. The period referred to in Article 5(6) of Decision 1999/468/EC shall be set at three months.

4. The Committee shall adopt its rules of procedure.

Article 31

Consultation of scientific committee

The Commission may consult the relevant scientific committee when adapting the Annexes of this Directive to scientific and technical progress.

CHAPTER VII

FINAL PROVISIONS

Article 32

Transposition

1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than .... They shall forthwith inform the Commission thereof.

When Member States adopt these measures they shall contain a reference to this Directive or shall be accompanied by such reference on the occasion of their official publication. Member States shall determine how such reference is to be made.

2. Member States may decide for one year after the date laid down in the first subparagraph of paragraph (1), not to apply the requirements of this Directive to tissue banks operating under national provisions before the entry into force of this Directive.

3. Member States shall communicate to the Commission the texts of the provisions of national law that they have already adopted or which they adopt in the field governed by this Directive.

Article 33

Entry into force

This Directive shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Communities*.

Article 34

Addressees

This Directive is addressed to the Member States.

Done at Brussels, [...]

For the European Parliament
The President
[...]

for the Council
The President
[...]

ANNEXES

Annex I. - Requirements for the procurement of human tissues and cells.

Annex II. - Quality management system.

Annex III. - Information to be provided on the donation of cells and/or tissues.

Annex IV. - Selection criteria for the donor of tissues and/or cells.

Annex V. - Laboratory tests required for donors

Annex VI. - Cell and/or tissue procurement procedures and reception at the tissue bank.

Annex VII. - Tissues and cell processing, preservation and distribution.