OPINION OF THE EUROPEAN GROUP ON ETHICS
IN SCIENCE AND NEW TECHNOLOGIES
TO THE EUROPEAN COMMISSION

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ETHICAL ASPECTS OF HUMAN TISSUE BANKING

Reference: Initiative of the Group

Rapporteur: M. Octavi Quintana-Trias

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THE EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES (EGE),

- Having regard to the Treaty on European Union as amended by the Treaty of Amsterdam, and in particular Article 6 (formerly Article F) of the common provisions, and the new Article 152 (formerly Article 129) of the EC Treaty on public health, and in particular paragraph 4(a) referring to substances of human origin;
- Having regard to Council Directive 89/381/EEC of 14 June 1989 extending the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products and laying down special provisions for medicinal products derived from human blood or human plasma;
- Having regard to Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products, and in particular its 6th amendment of 1993;
- Having regard to Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, and the proposal of 19 April 1995 for a Directive on in vitro diagnostic medical devices amending Directive 93/42/EEC;
- Having regard to Directive 95/46/EC of the European Parliament and of the Council of the European Union of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data;
- Having regard to the Resolution of the European Parliament on prohibiting trade in transplant organs (A3-0074/93) of 14 September 1993, and in particular point 2 thereof, which calls for a ban on imports, use and/or transplants of organs and tissues whose origin and state of health is not known with certainty;
- Having regard to Recommendation R(94) 1 of the Committee of Ministers of the Council of Europe on Human Tissue Banks adopted on 14 March 1994;
- Having regard to Resolution (78) 29 of the Committee of Ministers of the Council of Europe on harmonisation of legislation of Member States relating to removal, grafting and transplantation of human substances, adopted on 11 May 1978;
- Having regard to Recommendation (79) 5 of the Committee of Ministers of the Council of Europe to Member States concerning international exchange and transportation of human substances, adopted on 14 March 1979;

- Having regard to the Council of Europe Convention on Human Rights and Biomedicine, signed on 4 April 1997;
- Having regard to the Universal Declaration on the human genome and the rights of man adopted by the UNESCO on 11 November 1997;
- Having regard to the various laws and rules applying in some Members States concerning human tissues or organs;
- Having regard to the round-table that the Group organised with Members of the European Parliament, experts, representatives of industry, research, professional associations and patients on 27 November 1996, and to the hearing of experts and Commission departments on 17 March 1998;
- Having heard the rapporteur Mr O. Quintana-Trias,

1. WHEREAS:

1.1 What are human tissues?

Human tissue is defined as a functional group of cells.

For the purposes of this Opinion, human tissues means constituent parts of the human body such as: bones, skin, heart valves, cornea, tendons, arteries, veins, dura mater as well as foetal tissues obtained following abortions, placenta and umbilical cord (the cord itself and the cells it contains).

The Opinion also covers cells intended for grafting (in particular for somatic gene therapy and cell therapy), cell lines from cell cultures as well as cells used to produce proteins and other substances (e.g. monoclonal antibodies).

1.2 Parts and products of human origin not covered by this Opinion

This Opinion does not cover organs for transplantation, which are already covered by comprehensive, detailed national legislation in all Member States of the European Union.

Neither does the Opinion cover:

- blood and blood products, which are currently covered by national rules and by Community rules pursuant to the above-mentioned Directive of 14 June 1989;

- hair, nails, breastmilk and body waste (urine, sweat, saliva), which are treated differently because their removal does not give rise to major ethical problems;

- gametes, reproductive tissues (such as ovaries) and embryos, which are covered by specific national rules and give rise to quite specific ethical problems.

Every stored tissue is a potential source of genetic information (DNA). However, this Opinion does not cover genomic banks (DNA banks or "biobanks"), which give rise to many important legal and ethical questions (particularly as regards the confidentiality of data, access to such data, and possible uses even in the very long term). The Group intends to consider these in a subsequent Opinion.

1.3 Various uses of tissues

This Opinion covers a wide variety of human tissues, which can be used for a wide variety of purposes:

- for diagnostic purposes: e.g. to determine whether a tumour is cancerous or not by removing tissue (biopsy). In order to establish the cause of death, forensic medicine also analyses human tissues. Likewise, human tissues are the subject of toxicological studies to test the effects on them of certain products: insecticides, cosmetics, medicines;

- for therapeutic purposes: in this case, tissues are mostly used for transplantation. For example, orthopaedic surgery uses fragments of bone, while skin grafts are used to treat burn victims or as dressings in the treatment of diabetics. Tissues are also used as sources of proteins or other therapeutic substances. Today they are only very rarely used as sources of hormones in the European Union;

- for research purposes: basic, epidemiological and clinical research. Such research has, for example, made it possible to establish a link between asbestos and a lung cancer.

Nevertheless, tissues may no longer be used to make non-medicinal products. The use of human tissues in the manufacture of cosmetics was banned in Europe by the above-mentioned Directive on the approximation of the laws of the Member States relating to cosmetic products of 1976, which was amended in 1995, and applies in this respect from 30 June 1997. The Directive gives as grounds for the ban the risk of transmission of "Creutzfeldt-Jakob disease, human spongiform encephalopathy, and certain viral diseases".

1.4 Origin and removal of tissues

The most common source of human tissue is removal from the body as part of diagnosis or treatment. It may be affected tissues or surplus tissues, mainly surgical residues.

Tissues are also frequently removed from dead donors. Other sources include foetal tissues obtained following abortions (spontaneous or induced), as well as placenta and umbilical cords obtained at childbirth.

Exceptionally, tissues may also be obtained from healthy volunteers (skin, for example).

Tissues are generally removed or obtained in health care institutions or medical analysis laboratories.

1.5 Tissue banks

Unlike organs, which cannot be conserved, tissues can easily be stored for long periods. Once removed or collected, tissues are subject to a series of operations which, particularly when they are intended for transplantation, comprise the following functions:

- processing
- preserving and storage
- registration (to collect the data which will enable in particular the source of the tissues to be traced)
- distribution and delivery.

These are the functions performed by "tissue banks". Tissue banks are units or services which may be operated by public or private, profit-making or non-profit-making bodies (hospitals, blood transfusion centres, and even, in some cases, large laboratories ...).

At present there is insufficient information on tissue storage and distribution conditions across Europe, as no general inventory of human tissue banks has been made.

1.6 Processing of tissues

The processing of tissues is primarily intended to enable them to be preserved and stored in tissue banks. Where the tissues are intended for transplantation into another person, processing also includes clinical, microbiological and immunological tests intended to safeguard the safety of the recipient. These tests are intended to prevent the transmission of infectious, neoplastic (cancer) and immunological diseases.

Tissues collected for diagnostic or research purposes are generally studied in their original state in order to identify the illness affecting them.

Products can also now be obtained by increasingly sophisticated techniques which enable certain properties of the tissues to be modified. To that end the tissues undergo prior processing. This is the case in particular for skin cultures, which enable large areas skin to be made available for grafting.

1.7 Distribution of tissues

It is the function of tissue banks to organise the distribution of tissues to the professionals who will be using them for various purposes.

1.8 Main ethical issues

Wherever tissues are removed from human beings, and possibly transplanted into other human beings, the activities involved in the collection and use of such tissues are subject to ethical requirements intended to safeguard respect for human beings, their dignity and autonomy, and for the common good.

The issue of safety is also vital, as the European Union has set itself the objective of guaranteeing each citizen a "high level of human health protection". This protection must extend to tissue donors and recipients, and to all health care professionals - whose work involves collecting, manipulating and using human tissues.

At present we cannot be sure that the health safety of tissues is properly ensured throughout the European Union. This is due to the shortcomings of the existing national rules. As a result tissues move freely within Europe and are sometimes even imported from non-member countries, in many cases without detailed information on their origin, and in particular on the state of health of the donor.

1.9 Protection of the donor and the recipient

With regard to the removal of tissues, the main ethical principles from the donor's point of view are:

- respect for the human body, even after the person's death;
- respect for the autonomy of the donor; thus, tissue may not be removed whenever the person refuses. For deceased persons, this implies that tissues may not be removed if the person refused consent during her/his lifetime;
- protection of vulnerable people, namely people unable to give consent;
- respect for private life and medical confidentiality, which is a fundamental right;
- the right to prior information on the conditions of removal and the expected use of the tissues;
- the right not to be subjected to unfair discrimination, which could result from the revelation of data collected from the donor, or the family, to third parties (e.g. employers and insurance companies).

The main principles affecting recipients of allografts are:

- respect for the autonomy of the person concerned, which requires clear information on the risks and advantages of the proposed transplant;
- respect for private life and medical confidentiality, which applies to all medical treatment;
- the right to safety, which requires prior verification of the quality and safety of the tissue to be transplanted with regard to the risk of transmission of infectious diseases, neoplasms and immunological diseases;
- the right of patients to have fair access to the therapeutic possibilities offered by the transplantation of human tissues; the effectiveness of this right depends partly on the greater or lesser availability of tissues.

1.10 The problem of commercialisation of human tissues

All Member States of the European Union adhere to the principle that donations of human tissues must be free, following the example of blood, and this rules out any payment to the donor. However, the donor may receive compensation for the constraints associated with tissue removal (e.g. travel expenses, loss of earnings, etc.). Some parties maintain that for the sake of fairness, when the tissues become even indirectly a source of profit, donors should be paid. Furthermore, donor's remuneration might increase the supply of tissues. So far, however, the arguments in favour of the altruistic nature of tissue donation (like organ donation) have prevailed. They are based on a regard for solidarity. Also they are inspired by the desire to avoid the human person being regarded as an object (a source of organs and tissues). Another argument in favour of free donations is to avoid all risk of exploitation of the most underprivileged who might be led, in doubtful conditions of health, to donate tissue exclusively or primarily for financial reasons.

As an example, a debate arose a few years ago in the United States with regard to the removal of tissues from an individual whose cells had rare features (the Moore case). These tissues, ostensibly removed as part of a medical treatment, had in reality enabled profitable industrial applications, and this information was withheld from the donor. The deficient and misleading information given to the donor was condemned by the Court, even though the judge did not accept that Moore should participate in the economic benefit derived from the use of these tissues. However, this case leads some commentators to call for payments to be made to tissue donors for the sake of equity.

The issue of the commercialisation of human tissues which have been processed and prepared for therapeutic purposes is even more controversial.

For some, tissue banks must be operated only by non-profit-making bodies, as the tissues have originally been obtained free of charge in a spirit of altruism.

For others hold that the processing and conversion of tissues involve costs which they believe justify their commercial sale, in the same way as blood derivatives. The commercialisation of human tissues has the added advantage, according to its proponents, of encouraging industry to invest in areas which will result in greater availability of tissues on the market. This argument is most often advanced with regard to "engineered" tissues requiring sophisticated industrial processing techniques.

Currently, although no surveys of tissue banks in Europe have been carried out, it seems that most of the banks are non profit, nevertheless some of them have been set up by private industries, particularly for the production of engineered tissues.

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2. IN THIS CONTEXT, AND IN VIEW OF THE URGENT NEED TO REGULATE THE CONDITIONS UNDER WHICH HUMAN TISSUES CIRCULATE WITHIN THE EUROPEAN MARKET, THE GROUP SUBMITS THE FOLLOWING OPINION:

2.1 Ethical imperative to protect health

No substance of human origin is free from the risk of disease transmission. Thus 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.

To this end, the health safety rules to be drawn up at Community level must at least comprise:

* research on the personal, medical and family history of the donor in order to detect all possible transmissible diseases (e.g. to ascertain any occurrence in the donor of a subacute spongiform encephalopathy - Creutzfeldt-Jakob disease for which no valid test on living donors exists or a state of dementia before death that could be a symptom of this disease);

* thorough biological analyses according to recommendions of good medical practice in order to detect, for example, HIV viruses and, more generally, transmissible infectious diseases;

* any additional analyses that may be necessary in view of the donor's history or of the nature of the tissue in question.

The use of certain types of tissue for allografts or as a basis for the production of pharmaceutical substances should be banned or at least limited. This includes tissues whose safety cannot be proved due to the absence of valid tests (dura mater, auditory ossicles, tympanic and petrosal tissue used for grafting.)

Tissue retrieval should be supervised by a physician. In addition, all tissue procurement must be carried out by qualified staff under strict conditions (in particular, licensed premises which meet technical health standards).

The conduct of the necessary tests must be supplemented by surveillance mechanisms to detect any accidents and their origin at the earliest possible stage: donor documentation, monitoring of recipients, registers of accidents and remedial procedures in place. Such a surveillance and traceability system should be an integral part of the health rules drawn up at Community level.

The establishment of a European structure for the protection of health should also be envisaged, in collaboration with the European Agency for the Evaluation of Medicinal Products.

2.2 Body integrity

The integrity of the human body should be ensured when procuring human tissue from an individual, living or dead. When tissues are procured from the deceased, due regard should be paid for the feelings of relatives.

2.3 Information and consent

The procurement of human tissues requires, as a principle, the prior, informed and free consent of the person concerned. This does not apply in the case of tissue procurement ordered by a judge in the context of judicial, in particular criminal, proceedings.

While consent is a fundamental ethical principle in Europe, the procedures involved and forms of such consent (oral or in writing, before a witness or not, explicit or presumed, etc.) are a matter for national legislation based on the legal traditions of each country.

2.3.1 Living donors

In order to be informed, the donor's consent must have been given on the basis of information provided in as clear and precise lay terms as possible by the doctor supervising the procurement.

The information provided to the donor should concern:

* the procurement arrangements, in particular concerning the free nature of the donation, and the extent of its anonymity.

* possible tissue storage time and conditions, and conditions of registration of data in databases, in conformity with requirements of private life protection and medical confidentiality;

* foreseeable use of the tissues (diagnostic, allograft or autograft, pharmaceutical products, research, production of cellular lines for various uses, etc.). The donor may at any time withdraw her/his consent.

2.3.2 Deceased donors

Consent of a donor for retrieval of tissues after death may take different forms depending on the national systems ("explicit" or "presumed" consent). However, no retrieval of tissues may take place, with the exception of judicial proceedings, if the party concerned formally objected while alive. Furthermore, if there has been no expression of will and the applicable system is that of "presumed" consent, doctors must ensure as far as possible that relatives or next of kin have the opportunity to express the deceased person's wishes, and must take these into account.

2.3.3 Special cases

Special provision must be made in the following three cases:

- Foetal tissue procured after an abortion

No abortion should be induced for the purpose of obtaining foetal tissue. In the case of deliberate or spontaneous abortion, the retrieval of the tissue requires the specific free and informed consent of the woman and, where appropriate, of the couple. The timing of the termination and the way in which it is carried out must not be influenced by the retrieval of the tissues.

- Placenta and umbilical cord procured during delivery

The placenta can be an important source of vessels for transplant purposes. In these conditions, its procurement must be subject to prior information to the woman.

Umbilical cord may increasingly be procured because of its therapeutic interests. Umbilical cord blood banks are already being set up. The hematopoïetic stem cells in the cord blood may be useful, for example in the case of leukaemia, for autografts or allografts. In this respect, the information provided to the woman or to the couple must clearly explain these prospective new treatments, but stress that they are still very much at the experimental stage.

- Surgical residues

Surgical residues are currently one of the major source of tissues for allografts. Nonetheless, their procurement during operations (e.g. head of the femur, in the course of hip operations) is frequently unregulated.

The provision of information to the donor is all the more necessary today as the tests to verify the safety of the tissues can only be carried out with the consent of the donor.

2.4 Respect of privacy and protection of the confidentiality of information collected during tissue procurement

In the interests of anonymity, it is prohibited to disclose information that could identify the donor, and the recipient. In general, the donor should not know the identity of the recipient, nor should the recipient know the identity of the donor.

Procurement and storage of tissues in tissue banks leads to the collection and storage of a growing number of personal and family data. This is the case, for example, when tissues are stored following analysis for diagnostic purposes. It is also the case when tissues are removed for use in allografts, for health reasons. In the event of subsequent sanitary or health problems, there is a need to find the donor's identity and the medical file (traceability requirement).

In order to reconcile the traceability requirement and the need to protect the donor's rights (medical confidentiality and privacy), tissue banks must take the necessary steps to protect confidentiality of the data by developing appropriate coding systems.

2.5 Preventing possible discrimination

As with all health information, personal data relating to tissues stored by tissue banks may be the cause of unwarranted discrimination if revealed to third parties (in particular employers and insurance companies). Tissue banks must therefore take all appropriate steps to prevent misuse of the personal data at their disposal.

2.6 Promoting solidarity and tissue availability in Europe

Anonymous and free tissue donation - like organ donation - basically remains a voluntary act of solidarity. Therefore it is necessary in each Member State and at European Union level to encourage people to donate tissue as an act of solidarity. To this end, public should be given clear information on the conditions under which the donated tissues will be used and on the likely public health benefits. The information in question must also stress the specific responsibility of the tissue banks with regard to the safeguarding of ethical principles.

2.7 Role and responsibilities of the tissue banks

Activities of procurement, which are non-commercial, as well as activities carried out by tissue banks require an authorisation. This authorisation must be subject to compliance with basic ethical principles and with health safety standards, which themselves are an ethical imperative. Safety rules must be uniform throughout the European Union.

Tissue banks have an eminent responsibility to monitor implementation of these rules and principles. They should refuse to accept tissues the procurement of which does not satisfy ethical principles and safety rules.

Tissue banks also have specific responsibilities as regards protecting the confidentiality of the personal data they keep on donors and their families.

In view of their responsibility for the quality and safety of the tissues they provide to third parties, banks should be obliged to keep a register of the tissues stored and distributed. This register should be available for presentation to the national inspectorates at all times.

2.8 Profit or non-profit tissue banks

In principle, tissue bank activities should be reserved to public health institutions or non-profit-making organisations. In such case, this means that the delivery price of the tissues only covers 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 should be subject to the same licensing and monitoring requirements as non-commercial operators.

2.9 Towards equitable access to the therapeutic opportunities presented by the use of human tissues

The medical use of products of human origin is inevitably constrained by limited availability, owing to the precautions that have to be taken to guarantee safety and to the voluntary nature of donations.

According to the principle of justice, it is necessary to define the criteria for priority access to such tissue products in the most transparent manner possible, on the basis of an objective evaluation of medical needs, taking into consideration the objectives for public health in Europe.

2.10 Tissue imports from outside the European Union

Tissue imports or exports should be licensed by Public authorities. Authorisation should be subject to at least equivalent ethical and health rules to those outlined above.

2.11 Community survey on tissue banks

The European Union should promote periodic surveys in the Member States to obtain and diffuse data on practices relating to human tissues, from procurement to distribution, the organisation of tissue banks, particularly concerning the profit-making or non-profit making aspect and the true dimension of imports and import controls.

These surveys should be used to provide better information to the public on the ethical and safety controls in place, as well as on perspectives in therapy, diagnosis and research offered by uses with human tissues.

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