The European Group on Ethics
in Science and New Technologies
to the European Commission

Opinion on the ethical aspects of patenting inventions involving human stem cells

- Opinion N° 16 -

- 7 May 2002 -

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Delivered by the European Group on Ethics
In Science and New Technologies
To the European Commission

On 7 May 2002

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

No 16 **7 May 2002**

Original in English

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ETHICAL ASPECTS OF PATENTING INVENTIONS INVOLVING HUMAN STEM CELLS

Reference: Request by the European Commission on 18th October 2000
Rapporteurs: Linda Nielsen and Peter Whittaker

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The European Group on Ethics in Science and New Technologies (EGE),

Having regard to the request of Romano Prodi, President of the European Commission, to the EGE on the ground of Article 7 of the Council Directive 98/44/EC of 6 July 1998 on the legal protection of biotechnological inventions, giving mandate to the European Group on Ethics to evaluate "all ethical aspects of biotechnology";

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, concerning the respect for fundamental rights, Article 95C (formerly Article 100A) on the approximation of Law*, Article 152* (formerly Art. 129) on public health, Article 157 (formerly Art. 130) on Industry, and Article 163 (formerly Art. 130F) on Research and Technological Development;

Having regard to the Charter of 28 September 2000 on Fundamental Rights of the European Union, approved by the European Council in Biarritz on October 14th 2000, in particular Article 1 on "Human dignity", Article 3 on the "Right to the integrity of the person", which refers to the principle of "free and informed consent" and prohibits "the reproductive cloning of human beings", Article 13 asserting freedom of research and Article 17 which states that "intellectual property is protected";

Having regard to the Council Directive 98/44/EC of 6 July 1998 on the legal protection of biotechnological inventions and in particular Article 5, about the patentability of elements isolated from the human body, Article 6, concerning certain inventions excluded from patentability, and the above mentioned Article 7 giving mandate to the European Group on Ethics (EGE) to evaluate "all ethical aspects of biotechnology";

Having regard to the proposal for a Council Regulation on the Community Patent presented by the Commission on 5 July 2000;

Having regard to the judgement of the European Court of Justice of 9 October 2001, rejecting the appeal of the Kingdom of the Netherlands for annulment of the Directive 98/44/EC as well as to the opinion of the Advocate General of 14th June 2001 in this case;

Having regard to the European Patent Convention, signed in München in 1973 and establishing the European Patent Organisation, in particular Art. 52 on patentable inventions stipulating that discovery, as well as surgical, therapeutic or diagnostic methods for treatment of the human or animal body, are not regarded as inventions, and Art. 53.a concerning the exclusion from patentability of inventions the publication or exploitation would be contrary to "ordre public" or morality;

Having regard to the Budapest Treaty of the WIPO on International Recognition of the deposit of micro organisms for the purposes of Patent Procedure of 28 April 1977;

Having regard to the Trade Related Aspects of Intellectual Property Rights Agreement (TRIPS) annexed to the Agreement establishing the World Trade Organisation, entered into force on 1st January 1995, and in particular Article 27.2 concerning the exclusion from patentability of inventions the commercial exploitation would run counter to "ordre public" or morality, and Art. 27.3 concerning the exclusion from patentability of diagnostic, therapeutic and surgical methods;

Having regard to the Council of Europe's Convention on Human Rights and Biomedicine, signed on 4 April 1997 in Oviedo, in particular Article 15 about freedom of research, Article 18.2 prohibiting the production of embryos for the sole purpose of research and Article 21 stating that "*the human body and its parts shall not, as such, give rise to financial gain*";

Having regard to the Universal Declaration on the Human Genome and Human Rights endorsed by the United Nations on 11 December 1998, in particular, Article 11 which recommends to prohibit "reproductive cloning of human beings" and Article 12 b) which proclaims freedom of research as "part of freedom of thought";

Having regard to national regulations on patent and to ethics bodies opinions on stem cell research and their use;

Having regard to the previous EGE Opinion N° 3 of 30.09.1993 on the Commission proposal for a directive on biotechnological invention, Opinion N° 8 of 25.09.1996 on the patenting of inventions involving elements of human origin, Opinion N° 12 of 23.11.1998 on Human embryo research, and Opinion N° 15 of 14.11.2000 on Human stem cell research and use;

Having regard to the Round Table organised by the Group on 20 November 2001 in Brussels with members of the European Parliament, jurists, philosophers, scientists, representatives of industries, representatives of religions, representatives of patients' associations and other groups of interest, and of international and European organisations (UNESCO, Council of Europe, WTO, WIPO, EPO);

Having regard to the Hearings of experts on 3rd July 2001, 4th September 2001, 2nd October 2001, and 8th January 2002;

Having regard to the reports asked by the Group to Prof. Daniel Kevles (Department of History, Yale University) on "A history of patenting life in the United States with comparative attention to Canada and Europe" and to Prof. Geertrui Van Overwalle (Centre for Intellectual Property Rights, Faculty of Law, K.U. Leuven) on "Study on the patenting of inventions related to human stem cell research";

Having heard the rapporteurs Linda Nielsen and Peter Whittaker;

1. WHEREAS :

SCIENTIFIC BACKGROUND

1.1. Characteristics of stem cells

Stem cells are cells found in all vertebrate animals, including human beings. They play roles in the processes of normal development and regeneration or repair of damaged tissues.
The reason for this is their properties of dividing to give cells either identical to themselves or differentiated into particular types of cells.

Because of these properties, it is thought probable that stem cells will find use in the therapy of degenerative diseases or injuries. Other potential applications for human stem cell cultures include uses for studying fundamental processes of human development or for toxicological testing and drug design. Non-human animal stem cell lines may also be used to produce genetically modified animals. It is also possible that genetically modified non-human animal stem cell lines may be developed for human therapeutic purposes.

1.2. Sources of human stem cells

Different types of stem cells can be distinguished according to the sources from which they are retrieved. Thus, there are:

- **Adult stem cells:** progenitor and multipotent stem cells are present in adults. Mammals appear to contain some 20 major types of somatic stem cells that can regenerate the various tissues but they are rather difficult to find and isolate and they do not seem to have the same developmental potential as embryonic or foetal stem cells.

- **Stem cells of foetal origin:**
  - Haematopoïetic stem cells can be retrieved from the umbilical cord blood.
  - Foetal tissue obtained after pregnancy termination can be used to derive multipotent stem cells like neural stem cells which can be isolated from foetal neural tissue and multiplied in culture, though they have a limited life span. Foetal tissue can also give rise to pluripotent EG cells isolated from the primordial germ cells of the foetus.

- **Stem cells of embryonic origin:** pluripotent ES cells are those which are derived from an embryo at the blastocyst stage. Embryos could be produced either by in vitro fertilisation (IVF) or by transfer of an adult nucleus to an enucleated egg cell or oocyte (somatic cell nuclear transfer – SCNT).

  One can distinguish:
  - Embryos created by in vitro fertilisation. They can have been created for the purpose of assisted reproduction but not used for it (the supernumerary embryos) or they can have been created specifically for the purpose of research or treatment. These embryos are viable and could lead to birth if implanted in the uterus.

- Embryos created by cloning technique (by transfer of the nucleus of somatic cell into an oocyte) or created by parthenogenesis (by stimulation of an oocyte to initiate the duplication of the oocyte genetic material and then the division of the cell). Given the consensus in Europe to ban reproductive cloning, these embryos cannot be implanted in a uterus. Their capacity to lead to a birth is supposed to be either probably very reduced (in the case of the cloned embryo) or quasi-null (in the case of parthenogenesis).
- Stem cells may possibly be also obtained by injecting stem cell or egg cytoplasm into somatic cells transforming them into stem cells (ooplasmic transfer).

- **Other methods**: new technical ways of deriving stem cells may be developed in the future.

1.3. Derived cell and stem cell lines

One should distinguish:

- **stem cells freshly derived** from an organ or tissue which have not yet been subjected to any modification and which are capable of being propagated as stem cell lines,

- **unmodified stem cell lines** which refer to cultured lines of cells which have been propagated originally from freshly derived stem cells and which have not been modified in any other way. When the stem cells are derived from an embryo, the undifferentiated stem cell lines which can be derived from them are pluripotent.

- **modified stem cell lines** which refer to cultured lines of cells, propagated from stem cells or stem cell lines, which have been modified either by genetic manipulation, or by treatment that causes the cells to differentiate in a particular way.

LEGAL BACKGROUND

A. GENERAL BACKGROUND

1.4. What are the purposes of patent law?

- **Patent law in general**

  Patent law aims to promote technical innovation and the dissemination of its fruits. The inventor gets exclusive rights to control commercial exploitation of his invention for some years and in return, he discloses detailed description of his invention, making the new knowledge available to all. This disclosure enables others (researchers etc…) to build on the achieved knowledge.

- **European Directive**

  The original purpose of the 1998 EU Directive regarding legal protection of biotechnological inventions is to establish legal certainty in this area within the European Community and to help European biotechnological companies to become more efficient in promoting innovation and thus attracting investment.

In addition, the Directive includes ethical considerations which take into account specific concerns. In this aspect, the EU approach of patenting in biotechnology differs from the US legal framework in that field which does not explicitly refers to ethics.

1.5. What is a patent?

A patent provides the patent holder with protection, for a period of 20 years in general, against the commercial exploitation of the invention by others. A patent is not a legal title granting its holder the exclusive right to exploit his invention, nor is it a right of ownership. A patent is a legal title granting its holder the exclusive right to stop others from using or making his invention. If a third party wants to use an invention protected by patent, a licence is normally required from the owner of the patent.

The granting of a patent is not an authorisation for the use of the invention. As mentioned in recital 14 of the Directive .."*a patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial or commercial purposes*". Whether or not research, commercial use or marketing is permitted, may be dealt with by other kinds of regulation than the patent regulation.

1.6. What may be the scope of a patent?

A patent application contains a description of the invention and one or more claims. The claim(s) are an essential part of the patent as they define the scope of the rights given by the patent to the patent holder. The claim defines thus what third parties may or may not do without a licence from the patent's holder. A licence is normally based on paying a fee.
One distinguishes claim on product and claim on process or method:

- **A product claim** may concern a substance (like a chemical compound) or a composition of matter (like a cell line). The protection given by such patent includes the right to prevent third parties not having the owner's consent from making, selling, using or importing the said product;

- **A process claim** concerns the activities exercised upon for instance biological material to effect a process or a method. The protection given by such patent includes the right to prevent third parties not having the owner's consent from using the process, and using, selling or importing the product obtained by this given process. The protection does not cover the same product which would have been obtained otherwise.

Thus a product claim provides stronger protection for the patent holder and more restrictions in relation to further use and research than a process claim.

1.7. Who grants a patent?

Patenting facilities (National Patent Offices) are available in most countries (for instance the U.S.P.T.O[1]., I.N.P.I.[2] for France). The protection of the invention is limited to the state that grants the patent and the legal consequences of the patent are settled by the national courts.

[1] U.S.P.T.O.: United States Patent and Trademark Office
[2] I.N.P.I.: Institut National de la Propriété Industrielle

In 1973, the European Patent Convention (EPC) was signed in München, creating the European Patent Organisation (EPO). At present, 20 European countries including all 15 EU Member States have signed the EPC. A patent granted by the EPO may be registered in any of the states adhering to the Convention, avoiding then for the inventor the multiplication of applications. The EPO has recently incorporated the 1998 EU Directive within its practice.

In case of dispute over a patent, only the national courts are competent and thus may adopt diverging positions on the same dispute. Therefore, the European Commission proposed to create a "Community Patent", which would be delivered by EPO, and a centralised Community tribunal in the framework of the European Court of Justice would be set up to deal with the potential disputes. This Commission Proposal is still under discussion.

1.8. Criteria for a patent

A patent may be granted in all European countries, provided that the three following requirements are all met:

- **Novelty**. The invention must represent an advance in what is considered to be the "state of the art" in its field.
- **Inventive step**. The invention must not be obvious to anyone familiar with the field concerned. A simple discovery cannot constitute a patentable invention. One of the main difficulties regarding patenting in biotechnology, is the ability to distinguish between a simple discovery which is not patentable and an invention as such, which is patentable. As emphasized in the EGE Opinion N° 8 of 25.09.1996 on the patenting of inventions involving elements of human origin : "*The traditional distinction between discovery (not patentable) and invention (patentable) involves, in the field of biotechnology, a particular ethical dimension...*".
- **Industrial application**. The invention must be capable of industrial application. In this respect medicine and agriculture are considered to be "industry".

1.9. Exclusions

- **Traditional exclusions in Europe**

  In Europe patents are excluded if their publication or exploitation is in conflict with the "ordre public" or morality. The concept refers mainly to the respect of human dignity which is at the roots of human rights and is mentioned in the Article 1 of the Charter of Fundamental Rights. The Convention of München refers to "ordre public" in its Article 53.a and the 1998 EU Directive regarding legal protection of biotechnological inventions refers to "ordre public" and morality in its Article 6.

  Diagnostic, therapeutic and surgical methods are also traditionally excluded from patenting. This exclusion was aimed to maintain the sharing of medical knowledge and know-how for the benefit of patients. It does not concern products or drugs used for medical purposes.

- **Specified exclusions**

  The EU Directive goes into detail to specify what is contrary to "ordre public" and morality in the biotechnology sector, namely Article 6 states in particular that the following are considered to be unpatentable:
  "

  - *Processes for cloning human beings;*
  - *Processes for modifying the germ line genetic identity of human beings;*
  - *Uses of human embryos for industrial or commercial purposes;*
  - *Processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes."*

It should be noted, as stressed in Recital 38, that this list is "*to provide national courts and patent offices with a general guide to interpreting the reference to "ordre public" and morality … and obviously cannot presume to be exhaustive".*

1.10. Exemptions

In Europe, there is a traditional academic exemption, mentioned in most national laws, which allows further research without paying a licence to the inventor, if this research is not commercial.

1.11 Compulsory Licences

As stated in most national regulations and in the above-mentioned WTO TRIPS agreements, compulsory licences may be granted if the patent protection is contrary to the common good.

1.12. Differences between Europe and the US concerning patent in general

There are four main differences between EU and US regarding law or conception of application of the law:

- **Priority of the first inventor or the first claimer**

  While disclosure or previous claim by an inventor ends any right to later patent in Europe, the American system grants the patent right to the first inventor. After disclosure the inventor has a period of time - the so-called grace period - to claim the patent.

- **Exemption and exclusion**

  In the US, the legislation does not provide for academic exemption. But in practice, there are often agreements between patent owner and research laboratories, although it is not a right.

  In the US there are no legally based exclusions regarding diagnostic and therapeutic use or ethically based exclusions.

- **Criteria of patentability**

  The criteria for patenting are traditionally interpreted in a more flexible and broader way in the US, leaving a larger place for legal interpretation and for negotiation after the patent is awarded.

  In the US, the conception of what is an invention is broader.

  In the US, the invention must prove to have a "utility" instead of "industrial application", the notion of "utility" is less specific, it means it is useful. The conception of what is "useful" is broader than the more precise requirement of industrial application used in Europe.

- **Opposition to a patent**

  The possibility to oppose to a patent differs between the US and EU. In the US, only third parties whose interests are directly damaged by a patent can oppose via the US Patent Office or via a court, while in Europe, any person may oppose to a patent delivered by the European Patent Office by addressing directly the EPO, or via a court.

The need to translate patent applications in different languages makes also the cost of the patent much higher in Europe than in the US.

1.13. Patents and Transparency

The inventor is required to publish full details of the invention in a manner sufficiently clear and complete for it to be carried out by a skilled person. When a patent has been granted patent information is provided. There are comprehensive databases with international coverage, also accessible through the Internet. Moreover, there are patent databases with national coverage and bibliographic databases covering the literature.

B. PATENTING BIOTECHNOLOGICAL INVENTIONS

1.14. When were biotechnological inventions first patented?

In 1980, the US Supreme Court overturned its previous case law to allow the granting of a patent on living matter, namely an oil degrading bacterium (Diamond v. Chakrabarty's case law). But previously in the 70's, other biotechnological inventions have also been patented with regard to methods, such as in particular methods of recombinant DNA.

Since then, there is a standing practice for patenting biotechnological inventions on living matter. Thousands of patents consist of living matter, for instance micro-organisms, genes, cell lines including human ones such as cancer cell lines, and there are recognised ways to patent such inventions.

1.15. What is specific to certain biotechnological inventions?

As mentioned above, in the field of biotechnology, the distinction between invention and discovery may be less obvious than in other fields. Furthermore, the description of the patented product may also be difficult. That is why, with regards to micro-organisms, it is not enough to describe the micro-organism and its industrial application, so the deposit of the micro-organism may be necessary.

Therefore, the Budapest Treaty signed in 1977 and implemented by the World Intellectual Property Organisation defines how the written description of the invention must be supplemented by the deposit of the new micro-organism in an internationally recognised depository authority. The access to the micro-organism is defined by the national law of the country where the depository authority is.

1.16. Patents on stem cells

Worldwide there have been over 2000 patent applications involving human and non human stem cells, of which one quarter refer to embryonic stem cells. Over one third of all stem cell applications and one quarter of all embryonic stem cell applications have been granted.

According to the practice in the US or in the EU, the various processes which have been considered for patenting include:

- Processes for isolation of stem cells from embryos or tissues;
- Processes for enrichment of stem cells in mixtures of cells;
- Processes for culturing of stem cells;
- Processes for genetically modifying stem cells for particular applications. For example it may be possible to modify stem cells to avoid rejection following transplantation;
- Processes for inducing stem cells to differentiate in particular ways. It will be necessary to induce stem cell cultures to differentiate into particular types of cells (e.g. neural cells, heart muscle cells) for specific regenerative therapies;
- Processes for inducing adult stem cells to undergo 'retrodifferentiation' or 'transdifferentiation'. Retrodifferentiation refers to the induced reversion of adult stem cells, with limited differentiation capacity towards multipotency or pluripotency. Transdifferentiation is the induction of adult stem cells to differentiate into cells of a tissue type different from that normally associated with the particular stem cells;
- Processes to create embryos by transfer of a somatic cell nucleus to an enucleated egg (cloning technique) for derivation of stem cells. This provides the possibility for producing autologous stem cells which are less likely to be rejected;
- Processes to create non-viable "embryos" by parthenogenesis. These techniques, which may also be used to provide autologous stem cells, would eliminate the need to destroy potentially viable embryos for deriving stem cells;
- Processes for transforming somatic cells directly into stem cells, eg. by injecting them with stem cell cytoplasm or egg cytoplasm (ooplasmic transfer);

and the various products which have been considered for patenting include:

- Stem cells;
- Stem cell lines;
- Differentiated stem cells;
- Genetically modified stem cells.

1.17. Patenting of human embryonic stem cells

Human embryonic stem cells have so far been both isolated and cultured in the US, Australia, India, Singapore, Israel and Sweden, and only cultured in the UK. The issue raised by the 1998 EU Directive is whether patents on human embryonic stem cells should be granted or not, and the question is still in discussion. The facts are that such patents have already been granted in the US.

One example is the US patent awarded to the Wisconsin Alumni Research Foundation (WARF), for human pluripotent stem cells derived from spare embryos created for infertility treatment. This broad patent covers both James Thomson's method of isolating human embryonic stem cells (ESC) and the five undifferentiated stem cell lines derived. That patent gives WARF control over who may work with its five stem cell lines and for what purpose. WARF decided to provide access against a nominal fee to academic researchers and access against a negotiable fee to other scientists. In return for its funding of James Thomson's research, the for-profit Geron Corporation was granted a licence agreement by WARF. Geron holds exclusive rights to develop the stem cell lines isolated at the University of Wisconsin into three specific differentiated stem cell lines for commercial purposes.

ETHICAL BACKGROUND

1.18. Historical aspects of patenting

Since its origin at the end of the XVIIIth century, modern patent law has had an ethical dimension. Its aim is indeed to define the conditions of a "social contract" between inventors and society at large. On the one hand, inventors are able to be granted financial rewards and thus to share profits with manufacturers and industrialists. On the other hand, inventors are obliged to disclose information on useful inventions, for the benefit of the public good. That means that the purpose of a patent is to strike a balance between different interests.

The patent system aims to keep a balance between the inventor's interests and the interests of society. That is why a fair balance between both interests, meaning that the scope of the claim of the patent must be proportional to the scope of the effectively described applications of the inventions, has an ethical dimension.

1.19 Ethical aspects of patenting in biotechnology in general

The patenting of biotechnological inventions, especially in the health sector, includes special ethical dimensions. The patenting of inventions to be used for therapeutic or diagnostic purposes may have an impact on access to health care. Concern has been expressed about the patent award by the EPO to Myriad Genetics for diagnostic tests for breast cancer and ovarian cancer. The claims include the genes BRCA1 and BRCA2. It is feared that the monopoly on the tests that this will create will result in unreasonable prices being charged with consequent reduced access to the tests. There are similar concerns expressed about the award to the Chiron Corporation of a patent granted in Europe for a combined HIV – Hepatitis C test kit. It seems probable that similar situations might arise in the stem cell area. Although patenting should encourage research, there is a fear that patenting of biotechnological inventions may entail excessive costs of research which would also impede access to health care. Moreover, since the description of an invention is not sufficient for a researcher to reproduce or improve it, it is important to make research biological materials accessible to the researchers.

1.20. Ethical aspects of patents involving human stem cells

The patenting of inventions involving human stem cells raises specific ethical questions related to fundamental ethical principles, namely:

- **The prohibition of making profits from the human body** and its elements, as stated by Article 3 of the Charter of Fundamental Rights, which is grounded on the principle of non-commercialisation of the human body. The donation of stem cells of human origin (adult, foetal or embryonic) must not give rise to payment of donors, apart from the justified compensation of constraints.
- **The principle of free and informed consent of the donor** which is also reflected in article 3 of the Charter of Fundamental Rights and in the Recital 26 of the 1998 EU Patent Directive stating "*Whereas if an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law".*

1.21. Ethical aspects of patents involving human embryonic stem cells

The Group is well aware that all procedures involving directly or indirectly the human embryo are controversial in the sense that they are based on presuppositions for instance concerning the beginning of human life and the question whether there should be an absolute or a relative protection of human life in its different stages. Political and legal decisions in these ethical matters may change the self understanding of what it means to be a human being in a given epoch and society.

The question of the dignity and the moral status of the embryo remains indeed highly controversial in a pluralistic society as the European Union. Those who are opposed to human embryo research, cannot, a fortiori, consider any patenting in that field. Among those who consider research on embryos ethically acceptable, some may feel great reluctance towards patenting the resulting inventions, while others consider patenting inventions derived from embryo research as acceptable, especially given their potential medical benefits.

Industrial and commercial exploitation of human embryos is excluded from patenting according to Article 6 of the above-mentioned 1998 EU Directive. This article leaves open the question of patentability of cells obtained from donated embryos, nor does it state precisely which embryos are subjected to this exclusion. Some consider that non viable embryos, which cannot lead to a birth, such as those created by parthenogenesis, or even by somatic cell nuclear transfer (cloning), are not covered by this exclusion.

When the question is about the patentability of the process which requires the use of human oocytes to produce stem cells by any means, there is a risk that women may be submitted to undue pressure to donate oocytes.

There is at present a tendency to accept double morality where there is no coherence between different positions adopted by one country. For instance, one could expect that to consider research on human embryos to derive stem cells as unethical, might imply the prohibition of the import for research of embryonic stem cells derived from human embryos as well as of the use of potential therapeutic applications resulting from such research, which is not always the case.

2. OPINION

2.1. SCOPE OF THE OPINION

According to the 1998 EU Directive on the Legal Protection of Biotechnological Inventions article 7: « *EGE evaluates all ethical aspects of biotechnology* ».

The Group has, in its Opinion No. 15 of 14th November 2000 on the ethical implications of human stem cell research and its uses, made recommendations, namely:

- to set up a strict public control by centralised authorities, on human embryo research where it is allowed;
- to take measures to prevent commercialisation of human embryos or cadaveric foetal tissue;
- to ensure the respect of ethical principles through the control of public authorities, concerning import of human stem cells, where allowed.

This present opinion deals with the specific ethical questions related to patenting of inventions involving human stem cells. The Group is aware of the fact that patents also involve many difficult and different questions of an economic and political nature, which may influence the way of dealing with patents, but has seen its task as providing an ethical focus on the question. The rapid development of biotechnology, especially the promise of stem cell research, makes it appropriate to consider and clarify some questions which could not have been taken into account when the 1998 EU Directive was drafted, given the state of the art at that time.

One option would have been to forbid patenting of stem cells or stem cell lines. The consequence of such an option would be the major slowing of this research field (except in case of a very unlikely large public investment), and the EGE opinion is that it would be contrary to public (and especially patients') interests. Moreover, the Group considers that it would be contrary to the EU choices as expressed by the 1998 EU Directive on patenting.

The Group finds that it is crucial to define the conditions required to patent, the limits of the patenting of human stem cells in relation to ethical considerations and the relevant processes securing ethical evaluation.

2.2. THE BASIC ETHICAL DILEMMA

EGE recognises the importance of patents as an incentive to innovation and as a reward to the inventor for openness and publishing the results.

One ethical dilemma arises due to the fact that patents can encourage scientific progress which can be used to the benefit of better health care, and at the same time, patents can also impair access to the health care due to the need of a licence to use them and to the fees that will have to be paid to the patent holder.

It is then necessary to secure the right balance between the inventor's interests and the society's interest – in the sense that one task for the community is to secure ethical principles and values in the context of possible conflicting interests of stake-holders, namely: patients and patients' associations, inventors and other researchers, donors, industry, investors, healthcare providers, and social insurance providers.

In order to be able to specify ethical limitations, a number of problems are to be considered, including:

- content of patents (process or product);
- various sources of stem cells;
- methods used to derive stem cells;
- protection of the donor;
- possible socio-economic consequences and philosophical implications of the patent system as applied to stem cells (further research**,** access to health care).

2.3. CONTENT OF THE PATENT

It is the opinion of the EGE that:

- Isolated stem cells which have not been modified do not, as product, fulfil the legal requirements, especially with regards to industrial applications, to be seen as patentable. In addition, such isolated cells are so close to the human body, to the foetus or to the embryo they have been isolated from, that their patenting may be considered as a form of commercialisation of the human body.
- When unmodified stem cell lines are established, they can hardly be considered as a patentable product. Such unmodified stem cell lines do not have indeed a specific use but a very large range of potential undescribed uses. Therefore, to patent such unmodified stem cell lines would also lead to too broad patents.
- Therefore only stem cell lines which have been modified by in vitro treatments or genetically modified so that they have acquired characteristics for specific industrial application, fulfil the legal requirements for patentability.
- As to the patentability of processes involving human stem cells, whatever their source, there is no specific ethical obstacle, in so far as they fulfil the requirements of patentability (novelty, inventive step and industrial application).

2.4. SOURCES OF STEM CELLS

Human stem cells may be adult (from living or deceased donors), foetal or embryonic stem cells. The derivation of stem cells raises different ethical questions, depending on the source of the cells. The Group considers that applicants for a patent involving human stem cells should declare which is the source of the stem cells.

As already stressed by the Group in the Opinion N° 15 of 14/11/2000 on the ethical aspects of human stem cell research, there are strong ethical concerns about the use of human embryos which require specific caution. These concerns are reflected in the 1998 EU Directive which states that processes which would lead to uses of human embryos for industrial or commercial purposes are contrary to "ordre public" and morality and not patentable.

The Group sticks to the strict application of the principle of non-commercialisation of human embryos, which is in line with the principle of non-commercialisation of the human body.

The Group considers that patenting of inventions allowing the transformation of unmodified stem cells from human embryonic origin into genetically modified stem cell lines or specific differentiated stem cell lines for specific therapeutic or other uses, is ethically acceptable, as long as the inventions fulfil the criteria of patentability, and in respect of the above-mentioned ethical principles.

2.5. THE QUESTION OF CLONING

The 1998 EU Directive states, in its Article 6, section 2, that « *processes for cloning human beings* » shall be considered unpatentable. In recital 41 cloning is defined as « *any process, including techniques of embryo splitting, designed to create a human being with the same nuclear genetic information as another living or deceased human being* ». This provision raises the question of the scope of the prohibition to patent processes of cloning human beings. The Group notes that the 1998 EU Directive does not bring clarification on the specific question to apply the prohibition of patenting only to reproductive cloning or also to cloning for stem cells.

The Group recalls that:

- the process used to create embryos by somatic cell nuclear transfer is the same in both reproductive cloning and cloning for stem cells but the destiny of the cloned embryos differs;

- the prohibition to create identical human beings by cloning is shared by all EU states, and mentioned in the Charter of Fundamental Rights and in the additional protocol to the Convention of Council of Europe and more widely shared in the world, as mentioned in the Universal Declaration on the Human Genome of UNESCO;

- there is a diversity of approaches between member states concerning cloning for stem cells.

As mentioned in its Opinion N° 15 of 14th November 2000 on Research on human stem cells, there are strong ethical concerns to be taken into account about cloning for stem cells. Therefore, considering these ethical concerns, and particularly the risk of instrumentalisation and commercialisation of the embryo, the Group calls for a cautious approach, excluding the patentability of the process of creation of a human embryo by cloning for stem cells. The Group stresses the urgent need to engage a public debate on that issue.

2.6. PROTECTION OF THE DONOR

When the donated cells may become part of a patent application, donors should be informed of the possibility of patenting and they are entitled to refuse such use. Apart from justified compensation, donors ought not to get a reward which could infringe the principle of non-commercialisation of the human body. These ethical requirements should apply as far as possible to imported stem cells.

2.7. PATENTS AND FURTHER RESEARCH AND DEVELOPMENT

Although the appreciation of the patentability of an invention in biotechnology as in other fields is a matter of a case by case evaluation by a patent office and eventually by a court, the Group again insists on the necessity to avoid the granting of too broad patents that would impair further research and development.

In the new area of stem cell research, the potential use is hoped to expand over time and stem cell lines may provide very important research tools. In addition to the academic exemption, it is essential to secure that patents on stem cell lines are not too broad, as this may have adverse effects on the aim to support further innovation to the benefit of health care. It is therefore the opinion of EGE that patents shall only be granted, when the patent claim refers to a specific and a sufficiently accurately described stem cell line and its industrial application. That involves a consistent relationship between a patent claim and the description of the invention.

2.8. EUROPEAN REGISTRY

The Group calls for the creation of an EU Registry of unmodified human stem cell lines, such registry which should include information on both ES (embryonic stem) and EG (embryonic germ) cell lines should be publicly accessible. Its aim would be to ensure transparency and thus facilitate access by the research community to the needed biological material for further research.

2.9. PATENTS AND ACCESS TO HEALTH CARE

The patent creates a control regarding commercial use. This raises questions as to the uses which are covered by the patent.

To secure that patent holders do not misuse their rights for example by charging unreasonable fees for the use of their inventions, EGE finds that the recourse to compulsory licence should be encouraged when the access to diagnosis and treatment is blocked by misuse of patent rights.

The EGE stresses the fact that it is the responsibility of the states to establish legal procedure for the delivery of compulsory licence and to examine if fair access to health care justifies such a procedure.

2.10. ETHICAL EVALUATION OF PATENT APPLICATIONS

According to Article 7 of the 1998 Patent Directive, the European Group on Ethics is charged with the evaluation of the ethical aspects of biotechnology in general.

Besides this general evaluation, the EGE considers that there may be also a need to make ethical evaluations in the course of the examination of patent applications involving specific ethical dimensions.

It would be desirable that such ethical evaluation becomes part of the review process of national patent offices or European Institutions like EPO and that advisory panels of independent experts are set up for that purpose.

EGE proposes that, in the course of the evaluation of biopatenting required by Article 16 of the 1998 EU Directive, specific attention is paid to the consequences of the patents on further research and access to health care, especially with regard to the fair and equitable accessibility of new therapeutic and diagnostic products at high costs.

The European Group on Ethics in Science and New Technologies:

The Chairperson : Noëlle Lenoir

The Members:

Rafael Capurro	Anne Mc Laren	Pere Puigdomenech Rosell
Yvon Englert	Göran Hermerén	Stefano Rodota
Linda Nielsen	Peter Whittaker	Günter Virt
Inez de Beaufort		

DISSIDENT OPINION:

Prof. Günter Virt agrees in general with the above, but does not agree permitting patenting processes and products using material resulting from destroyed human embryos:
"Human embryonic stem cells and also embryonic stem cell lines are excluded from patentability because we cannot get embryonic stem cell lines without destroying an embryo and that means without use of embryos. This use as material contradicts the dignity of an embryo as a human being with the derived right to life. If the condition for patentability is the industrial and commercial use and if the use of human embryos for industrial and commercial purposes is not patentable, then every exception, which cannot exclude industrial and commercial purposes, is against the ethical sense of the directive. Patenting is an incentive. Patentability of human embryonic stem cells and stem cell lines would push research towards embryonic stem cells and thus undermine the priority of research using non embryonic stem cells. Despite the relatively clear regulations in the directive this incentive for research will lead to forms of "bypasses" which makes it impossible to guarantee an ethically tolerable situation in the field of patentability".

THE PATENTABILITY IN THE EUROPEAN UNION

Jean-Luc GAL

National expert to the European Commission
DG Internal Market

Community Law
in relation to processes for the cloning and patentability
of inventions relating to the genome and certain humain cells

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Introduction[1]

Following the intensification of scientific research and the important discoveries made in the last forty years in the field of molecular biology, biotechnology has emerged as one of the most important and promising of techniques. The impact of processes, techniques and biotechnological material is felt in many sectors - health, agriculture, environment, food and industry.

However, in the mid-1980s, the diversity - and indeed the absence - of national laws on the subject proved detrimental to the research, development and competitiveness of European undertakings by comparison with Japanese or American companies active in this sector.

For these reasons, it has been vital that the European Community should launch an initiative in this sphere in order to harmonise national laws within the internal market.

The main reason for a proposed Commission directive was the total absence of any harmonisation within the internal market of the European Community.

This proved detrimental to the research, development and competitiveness of European undertakings by comparison with Japanese or American companies.

Hence, in 1985, the Commission White Paper on completing the internal market noted that:

> *"The differences in intellectual property laws have direct and harmful repercussions on intra-Community trade and on the capacity of undertakings to consider the intra-Community market a unique environment for economic activities [...] The picture has become even more complicated recently on account of the need to adapt existing intellectual property systems to the technological changes which have taken place in a number of fields, particularly that [...] of biotechnology [...] The Commission therefore intends proposing measures on the protection of biotechnological inventions to the Council." [Unofficial translation]*[2].

A need for clarification therefore made itself felt in this connection in order to establish clear and legally sound rules allowing industries of this type to develop harmoniously.

With this in mind, the Commission submitted an initial proposal for a directive on 21 October 1988[3]. In it, the Commission observed that:

> "*The system for protection by patent is essentially intended to encourage technical innovation, which is an important factor of economic growth, by recompensing the inventor for his creative work so as to stimulate inventive activity. Protection by patent therefore enables capital to be attracted to research/development and the industrial exploitation of research results while fostering the rapid and beneficial spread of knowledge otherwise liable to remain secret." [Unofficial translation].*

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[1] This article was made possible through the kind participation of Mr Erik Nooteboom, Head of the DG Internal Market, Industrial Property Unit/E2.

The author, Mr Jean-Luc Gal, is a national expert to the European Commission from the INPI (National Institute for Industrial Property). He works in the Industrial Property Unit.

The ideas and opinions expressed are entirely those of the author and cannot predetermine the opinion of the Commission or the INPI.

[2] Commission White Paper for the European Council in Milan (28-29 June 1985). The completion of the internal market, COM (85) 310 final, 14 June 1985, 6 145 *et seq.*

[3] COM (88) 496 final/SYN 159 of 21 October 1988, OJ No C from 10 to 13.1.1989.

This proposal was rejected on 1 March 1995[4] by the European Parliament following a conciliation procedure mainly on account of the lack of any distinction, in connection with DNA sequences, between discoveries which cannot be protected by a patent and true inventions which, for their part, can be covered by an industrial property right.

A new amended proposal was put forward at the end of 1996[5].

The opinion of the European Group on Ethics was delivered on 25 September 1996: this recognised that the traditional distinction between discoveries and inventions included an important ethical dimension in the biotechnology sphere. However, the opinion stressed that the directive did establish guarantees in this sphere.

The directive was finally adopted on 6 July 1998[6]. The Netherlands Government voted against this directive, while Italy and Belgium abstained. The directive was published in the Official Journal on 30 July 1998[7]. Article 15 lays down that the Member States must bring into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than 30 July 2000.

It should be noted that at the present time only three Member States have formally implemented the directive in their national legislation: Denmark, Finland and Ireland[8]. However, the great majority of countries have begun the legislative process which will lead them to the adoption, as rapidly as possible, of their internal legal instrument implementing the directive.

Finally, despite the appeal from the Netherlands to the Court of Justice[1], all the Member States are bound by the content of the directive and have been since the expiry of the transposition deadline[2].

It should be noted that the European Patent Office introduced the main provisions of Directive 98/44 into its Implementing Regulations following a decision by the Administrative Council of 16 June 1999[3].

It is important to note that protection by patent is currently afforded in the European Union by two systems, neither of which is based on a Community legal instrument: the European patent system and the national patent systems.

It ought similarly to be noted that the patent law applicable in the Member States originates in the convention on the unification of certain aspects of invention patent law signed at Strasbourg within the framework of the Council of Europe on 27 November 1963. This convention defines, in particular, the conditions of patentability and also lays down certain exceptions to patentability.

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[4] C4-0042/95 – 94/0159 (COD), Doc PE-CONS 3606/1/95 of 21.2.95. OJ No C68 of 20.3.95, p. 26.

[5] OJ C296 of 8.10.1996, p4, OJ C 311

[6] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, reproduced under the heading “Legislative texts and documents” in this publication.

[7] To be consulted on line: http ://www.ipr-helpdesk.org/t_en/i/i_410_en.asp?adt_id=749&ads=98

[8] Formal notifications received on 30 November 2000. The United Kingdom, which has already promulgated its regulation for the implementation of Directive 98/44, ought to notify this at any time now.

[1] Case C-377/98 of 30.10.1998, case pending.

[2] It should be noted that Article 242 of the EC Treaty provides that:
“Actions brought before the Court of Justice shall not have suspensory effect. The Court of Justice may, however, if it considers that circumstances so require, order that application of the contested act be suspended.
Pursuant to the second sentence in this article, the Kingdom of the Netherlands brought an appeal in order to obtain the stay of execution of Directive 98/44. By an order dated 25 July 2000, the President of the Court rejected this request”: see: http://curia.eu.int/jurisp/cgibin/form.pl?lang=fr&Submit=Rechercher&docreuire=alldocs& numaff=C-377%2F98&datefs=&datefe=&nomusuel=&domaine=&mots=&resmax=100.

[3] OJ EPO 7/1999, p. 437.

The content of the Strasbourg Convention was taken up again in the Convention on the Grant of European Patents concluded in Munich on 5 October 1973[4]. Today, 20 European States are party to this Convention[5], the aim of which is to establish a set of national patents governed by national and Community law via a unique procedure for the examination of a patent applications.

Hence a European patent entering its national stage and relating to a sequence of DNA will be subject to the provisions of Directive 98/44.

It is still desirable to be able to obtain, particularly in connection with biotechnology, a Community patent of a unitary nature valid in all the Member States of the European Community. It was therefore with this in mind that the European Commission submitted a draft regulation on the Community patent[6].

Directive 98/44 established a flexible legal framework in relation to the issues raised by the protection by patent of DNA sequences. Similarly, it endeavoured to propose certain legal guidelines covering the patentability of human stem cells, which is a sector in the process of full development.

I. Patentability of DNA sequences

The patentability of DNA sequences will be covered in three stages: at the outset, it is appropriate that attention be drawn to the issues at stake in connection with the human gene. The conditions for the patentability of these genes will then be looked at. Finally, the question of the scope of the rights conferred on biotechnological inventions and the limits which can be applied to those rights will be dealt with.

A. General presentation

The human genome is made up of a vast combination of DNA (deoxyribonucleic acid) sequences which contains both genes (coding DNA sequences which can give rise to proteins - see below) and a large quantity of DNA not having real known functions. Thus genes are dispersed within the genome.

It should be noted that a copy of the genome is to be found in most human cells.

DNA, which exists in its natural state in the human body, is made up of some three billion basic pairs (adenine, guanine, thymine and cytosine) which are coupled together (A and T, C and G).

DNA is the chemical basis of some 80 000 to 100 000 genetic code genes[7]. It is the order in which the basic pairs exist which constitutes the coded information of genes. Genes collectively gather together in the form of chromosomes representing the genetic pool of a living organism or cell. This pool is transmitted to the daughter cells and to the descendants of an organism.

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[4] A procedure for the review of the European Patent Convention was held in Munich from 20 to 29 November 2000. Conference documents may be consulted on: http://www.european-patent-office.org/epo/dipl_conf/documents_f.htm

[5] The fifteen Member States and also Switzerland, Liechtenstein, Monaco, Cyprus and Turkey.

[6] COM (2000) 412 final 1.8.2000.

[7] This is only an estimate since it is currently impossible to be able to establish a precise and definitive number of genes in humans.

The DNA of a cell is an internal stock of information which is not renewed or destroyed. When a gene's information has to be expressed, it must firstly be copied in the form of a molecule of messenger ribonucleic acid (m-RNA). The proteins are the products of the decoding of m-RNA's. The gene filiation → m-RNA → protein represents the genetic pool. Proteins are molecules which specifically execute the orders of genes. The code which allows the structure of a protein to be defined (the sequence of the amino acids) operates according to a universal correspondence system. It applies both in the case of bacteria and in the case of mammals: an amino acid corresponds to three successive bases. Nature has retained only twenty amino acids as players in the game of life. They are to be found in all living organisms.

It is these genes which are of real interest in the sphere of biotechnology and for which a type of specific protection is therefore required.

Precise Community rules therefore needed to be established in order to take these specific features into account, and this was done through Directive 98/44. However, the basic principles of patent law continue to apply in this field of technology.

Recitals 8 and 13 in Directive 98/44 clearly set out this situation. Recital 8 lays down that:

> *"Legal protection of biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national patent law; [...] the rules of national patent law remain the essential basis for the legal protection of biotechnological inventions given that they must be adapted or added to in certain specific respects in order to take adequate account of technological developments involving biological material which also fulfil the requirements for patentability."*

Recital 13 adds:

> *"The Community's legal framework for the protection of biotechnological inventions can be limited to laying down certain principles as they apply to the patentability of biological material as such, such principles being intended in particular to determine the difference between inventions and discoveries with regard to the patentability of certain elements of human origin, to the scope of protection conferred by a patent on a biotechnological invention [...]"*

B. Patentability of biotechnological inventions

1. Distinctions between patentable discoveries and inventions

The patent laws applicable within the Member States of the European Community generally contain a non-exhaustive list of what must not be regarded as an invention. The exclusions relate to constructions which are abstract (such as scientific theories or discoveries) or not of a technical nature (mere presentation of information).

An invention needs to be both practical and technical. In other words, it must provide a technical solution to a technical problem.

Thus if someone discovers a new property belonging to biological material which is already known, such as a DNA sequences in particular, that person only makes a simple discovery which is not in itself patentable.

However, if that same person is capable of determining a practical use of a technical nature attached to that property, he/she has then conceived an invention and can therefore file for a patent. Moreover, if a substance found in nature is isolated for the first time from its natural environment and if a process can be developed from it which resolves a technical problem, this process is therefore patentable.

To sum up, the essential factor which characterises an invention is its technological contribution. The same result would have been impossible to achieve without recourse to man, since nature is incapable of attaining the same result by herself.

In Directive 98/44, Articles 5(1) and 5(2), jointly with Recitals 20 and 21, lay down the existing distinctions between a simple discovery and a true invention.

Article 5(1) lays down that the simple discovery of an element of the human body, including a total or partial sequence of a gene, does not constitute a patentable invention.

Hence the directive is in accordance with Article 4 of the UNESCO declaration[8] on the human genome and the new Charter of Fundamental Rights of the European Union[9] which debars any financial gain being made from the human genome in its natural state.

Moreover, the joint declaration on the human genome presented by President Clinton and Prime Minister Blair is also based on the same approach to this issue. The conclusions of the Okinawa Summit under the auspices of G8 are also fully compatible with the provisions of Directive 98/44.

It is thus indisputable that neither the human genome nor a DNA sequence as such can be patentable according to the directive since they do not constitute inventions: they existed prior to being revealed. Admittedly, they have enabled human knowledge to be extended but this knowledge must be applied if it is to be technologically useful.

Hence the fundamental data on the human genome which it has been possible to reveal through the project christened HUGO (Human Genome Project), an alliance of public institutions and commercial companies, are not patentable. This is why patents must not restrict access to these fundamental data.

However the Directive, in Article 5(2), lays down that an element isolated from the human body or otherwise produced by means of a technical process, including the partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

Recital 21 in the directive reasons as follows: a DNA sequence can be the result of technical processes which identified, purified, characterised and multiplied it outside the human body. Such a process could not be conducted by nature alone.

2. The criteria of patentability

To obtain a patent on an invention based on, or included in, a gene, the general conditions of patentability need to be met: the invention must be new, show inventive activity and lend itself to industrial application.

[8] http ://www.unesco.org/ibc/fr/genome/projet/index.html.

[9] http ://www.consilium.eu.int/df/default_asp ?lang=fr. OJEC 364 of 18.18.2000, p. 1.

Moreover, the traditional laws relating to patent law generally comprise two additional patentability conditions:

- the invention must be of a technical nature, in other words it must lie within the technical sphere. In addition, it must relate to a technical problem. It must also possess technical characteristics and be able to be outlined in claims which allow the aim and scope of protection to be defined;
- in addition, the invention must be sufficiently described for the specialist to be able to reproduce it on the basis of the information contained in the patent application.

If these requirements are not met, the invention cannot be protected by a patent.

Article 3 of the Directive reiterates these basic principles concerning biotechnological inventions.

a. Novelty

The first criterion to be fulfilled is therefore novelty. This condition refers to the question of the state of the art.

The state of the art can be defined as follows: anything made available to the public by written, oral, electronic means or by use before the date of the filing of a patent application. In other words, if the invention is included in state of the art, it could not be protectable via a patent.

In the biotechnology sphere, it has occasionally been maintained that a gene could not meet this notion of novelty, insofar as it was present in certain data banks accessible to the public. However, the presence of a gene in a data bank is not sufficient to destroy the novelty of an invention. In fact, in the light of the data communicated, a person still needs to have had knowledge of the information to be capable of achieving the invention. This therefore means that the invention must be sufficiently accessible to the public for the nature of novelty to be no longer able to be fulfilled.

Directive 98/44 reaffirms this approach in Article 3(2), which states that:

"*Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.*"

This assertion is, moreover, clarified within Article 5(2) which deals in particular with the specific case of genes and DNA sequences.

b. Inventive activity

To be protectable, an invention must be of an inventive nature. Inventive activity must be comprehended in the light of the state of the art. Thus an invention will be deemed to satisfy the criterion of inventive activity if, in the light of the state of the art, it does not appear obvious to the specialist. It should be pointed out that the specialist is not an utterly inflexible institution and that, quite the contrary, he/she is infinitely variable depending on the technical sphere dealt with.

Thus, as far as biotechnology is concerned, he/she will be a person with an average knowledge of genetic engineering who, having regard to the state of the art (all the available knowledge), will be capable of making the invention described without recourse to a degree of creativity, or indeed extreme ingenuity. It is sufficient for him/her to be able to achieve the invention described by applying standard, known reasoning processes.

Article 3 of Directive 98/44 points out the requirement that this condition should be complied with in the sphere of biotechnology.

The concept of inventive activity is, quite obviously, a fluctuating one. Thus it should be pointed out that, while considerable efforts and resources had to be deployed at the beginning of any human genome sequencing operation to isolate and characterise the first genes, it seems that such processes have now proved to be less arduous. In certain cases, they can even be described as routine.

Our knowledge of genes is growing. We have an increasing knowledge of their functions within the organism and their relationship with specific diseases. Accordingly, there are those who now think that such processes have become mechanical and cannot therefore be protected by a patent.

In such instances, it is indisputable that such genes isolated and characterised almost automatically will probably be inventions (in other words, they will not be excluded, as such, from the scope of patentability) but for all that they will not be patentable. They will not, in fact, meet the essential criteria of inventive activity.

Moreover, some claim that it is the simplest matter to deduce the function of a gene by computer-aided simulations (bio-informatics) based on other genes whose functions are already known; this technique is described as research by homology.

If research by homology indicates that there is a broad similarity between the new gene examined and another one which is already known, it is therefore highly likely that the new gene possesses a function similar to that previously revealed in the already known gene. Accordingly, on the basis of information obtained via the first gene, the function of the new gene can easily be guessed.

In this case, patentability will not be able to be recognised in respect of such inventions on account of the absence of any inventive activity.

c. Industrial application

The criterion of industrial application is deemed to be fulfilled if the invention can be carried out or used in all spheres of industry, including agriculture.

Directive 98/44 does not challenge this requirement. On the contrary, it endeavours to provide clear guidelines in this particular sphere of technology.

There are those who have questioned the need for such specifications, when no such approach has been followed in respect of novelty or inventive activity. The reasons are simple: the approach to be followed in order to assess novelty or inventive activity in this sphere of technology could be the same as that adopted to address any other technical sphere.

Accordingly, the specifications in regard to the criterion of industrial application do not run counter to the principles laid down earlier for this condition of patentability: it was, by contrast, deemed by the legislature to be adequate to provide major specifications in order to be able to characterise this requirement.

Thus Article 5(3) lays down that the precise industrial application of a DNA sequence must be divulged for the invention to be protected.

Moreover, Recital 23 clarifies this requirement by stating that a DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention.

Recital 24 adds that where a sequence is used to produce a protein, it needs to be specified which protein is thus produced or what function it performs.

The degree to which the function requires to be divulged is going to vary from case to case. In fact, the importance of specific divulging will have to be assessed by the yardstick of the knowledge available when the application for a patent is examined. This requirement will become increasingly important as the therapeutic and diagnostic use of a gene becomes commonplace.

However, it seems to be virtually accepted that the mere isolation of a gene and any speculation on the potential function which that gene is capable of fulfilling do not appear sufficient to justify the issue of a patent.

3. Process of surgical or therapeutical treatment - further therapeutic application

It should be noted that a biotechnological invention can consist entirely of a surgical treatment process.

Article 27(3a) of the TRIPs Agreement[10] allows its members to exclude diagnostic, therapeutic and surgical methods for the treatment of human beings from patentability.

Thus Article 52(4) of the European Patent Convention (hereinafter EPC) is fully in accordance with that article by making express provision for the exclusion of such processes from the field of patentability.

In any event, Recital 35 in Directive 98/44 points out that:

> "*This Directive shall be without prejudice to the provisions of national patent law whereby processes for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are excluded from patentability."*

It may also be that a protein which has been coded on the basis of a DNA sequence can present a new function which is different from that initially planned in an earlier patent application. In this specific case, Recital 28 of the directive points out that:

> "*This Directive does not in any way affect the basis of current patent law, according to which a patent may be granted for any new application of a patented product."*[11]

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[10] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs Agreement) (1994), http ://www.wto.org/english/tratop_e/trips_e/t_agmO_e.htm.

[11] Here, too, the positive law applicable on the subject is essentially the European Patent Convention. Currently Article 54(5) of the EPC lays down that:

"The provisions of paragraphs 1 to 4 shall not exclude the patentability of any substance or composition, comprised in the state of the art, for use in a method referred to in Article 52, paragraph 4, provided that its use for any method referred to in that paragraph is not comprised in the state of the art."

The current conference for the review of the EPC plans to retain this article and add a new one which would read as follows:

"Nor do Paragraphs 2 and 3 rule out the patentability of a substance or composition referred to in Paragraph 4 for any specific use in any method referred to in Paragraph 53(c), provided that use is not included in the state of the art." *[Unofficial translation].*

This new wording allows full account to be taken of the second therapeutic indication and also the subsequent ones, although it leaves some doubt as to the exact scope of the first therapeutic indication.

C. Scope - Exceptions to the exclusive rights conferred on the holder of the patent

1. Scope of the patents covering DNA sequences

It should be pointed out that the general rules for assessing the scope of an invention relating to a DNA sequence continue to apply.

Thus Article 69(1) of the EPC can provide useful clarifications:

> *"The extent of the protection conferred by a European patent or a European patent application shall be determined by the terms of the claims. Nevertheless, the description and drawings shall be used to interpret the claims."*

However, Recital 13 of the directive states that specific details need to be provided concerning the extent of the protection conferred by a patent in the sphere of biotechnology.

Thus Article 9 of the Directive states that:

> *"The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product is incorporated and in which the genetic information is contained and performs its function."*

Moreover, Recital 25 states that:

> *"For the purposes of interpreting rights conferred by a patent, when sequences overlap only in parts which are not essential to the invention, each sequence will be considered as an independent sequence in patent law terms."*

Thus, the scope assigned to a patent relating to DNA sequences must be assessed in the light of these provisions.

2. Exceptions to the exclusive rights conferred on the holder of the patent

Concerning the authorisation to undertake experimental activities relating to inventions in the biotechnology sphere, reference needs to be made to national or European legislation. In fact, *the aim of the directive is not to state an opinion on the control of research*, as Recital 14 very appropriately points out.

However, it should be noted that all laws governing the patents of Member States within the European Community contain provisions authorising research into, and experimentation on, the field covered by a patent.

Moreover, even if these do not, on the face of it, appear to be desirable, forms of protection such as compulsory licences are provided for within the framework of the normal operation of patent law to ensure that the holder of the patent does not abuse the rights he/she enjoys.

Moreover, the point should be stressed that Directive 98/44 limits itself to determining solely what the subject of protection by a patent can be in the light of patent law. Hence patent law and, all the more so, Directive 98/44, have not adopted *ethical standards or values for reasons of ordre public or morality*. Directive 98/44 limits itself to drawing attention to the fact that certain inventions which could meet patentability criteria may be ruled out on ethical grounds, stemming from relevant national, Community or international laws. It limits itself solely to citing an indicative and non-exhaustive list.

A patent could not confer a positive right to use an invention. Such a use and, accordingly, the research and development leading to that invention continue to be governed by national and European laws.

Hence, Recital 14 points out that:

> *"A patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial and commercial purposes."*

The Directive has managed to establish a balanced position in relation to the patentability of DNA sequences taking into account the special nature of the field concerned, although also the interests of biotechnological companies.

II. Patentability of human stem cells

To begin with, it should be pointed out that what is incorrectly described as "therapeutic cloning" is in no instance intended to *reproduce human beings identically*[12]. The interest of this technique lies in the possibility of being able to recreate organs or tissues from cells which are described as "stem" and which have been able to be isolated, particularly during the initial stages of life of the embryo.

At the start of the third millennium, human stem cells appear to be particularly promising in the treatment of diseases which hitherto seemed as if they would remain incurable forever.

However, as these cells are extracted from the human being, they cause fear among some people and hope among others.

With the first steps these new techniques are taking, a brief technical overview ought to be given in order to classify the problems involved, followed by a study of the premises of the legal questions which are bound to arise in future years.

A. Technical overview

Human evolution illustrates this development very clearly. Human development begins when a spermatozoon fertilises an ovule and creates a single cell which has the potential to create an entire organism. This fertilised egg is *totipotent*.

[12] The reproduction of human beings identically is described as reproductive cloning. It is currently known that reproductive cloning techniques have only been used successfully among animals since the birth in Scotland of the sheep Dolly.

In the first few hours following fertilisation, this cell divides into identical cells which also retain the totipotent character.

This means that if one of these cells is placed in a woman's uterus, it will have the capacity to develop into an embryo.

Approximately four to five days after fertilisation, and after several cell division cycles, these totipotent cells begin specialising. A cavernous sphere forms within them which is termed a blastocyst. This blastocyst is composed of an external mass and an internal mass.

The external mass is the origin of the placenta and other issuing matter needed for the development of the foetus in the uterus.

The cells in the internal mass are not yet specialists and can give rise to virtually any human tissue, although it should be observed that, in themselves, these cells cannot create a human being insofar as they are incapable of creating a placenta, which is vital for the development of the embryo in the uterus.

These cells are described as *pluripotent* since they can give rise to any type of human body tissue. They cannot be described as an embryo because if they are placed alone in a uterus they cannot under any circumstances develop into a foetus.

These cells will continue to develop and finally give rise to specific cells fulfilling certain particular functions. Thus, blood stem cells situated in the spinal cord can give rise to red corpuscles, white corpuscles or platelets and can do so throughout the life of the human being. These more specialised cells are described as *multipotent*. They are extraordinarily numerous in the embryo, although found in far smaller quantity in the child and adult.

Currently, embryonic stem cells (i.e. pluripotent cells) have been able to be developed from two sources:

- The first method consists of isolating cells from the internal mass of the blastocyst. It has proved possible to cultivate these cells and obtain a line of cells from them which are described as *embryonic stem cells*[13]*;*

- The second method consists of isolating pluripotent cells from foetal tissues obtained following - in particular - an abortion. The cells which are to be removed are located in the testicles or ovaries. These cells are termed *Embryonic Germ Cells.*[14]

The scientific benefit of using embryonic stem cells is manifold.

- The study of stem cells ought to allow the complex succession of the phases observed during human development to be gradually understood;

- Recourse to stem cells could radically modify the practice observed for developing medicines. Using these stem cells to carry out the necessary tests before marketing future medicines can, apparently, be envisaged;

- The development of cell therapy seems to be the most ambitious objective. Numerous diseases are the result of dysfunctions of cell functions or the destruction of certain human body tissues.

Cell therapy has, indeed, been used for a number of years. It currently consists of replacing diseased cells or those which are insufficient in number by new cells. For example, the treatment of leukaemia or cancer by a bone marrow graft is a form of cell therapy. However, organ donations are generally insufficient to meet the demand.

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[13] More commonly described as ES cells.

[14] Or EG cells.

Moreover, cell graft techniques have limits: rejection occurs on account of immunological incompatibility, the lack of an organ donor, the absence of cells which can be grafted in the case of certain types of human tissue, etc.

Cell therapy using embryonic stem cells offers new and extremely interesting prospects for the future treatment of degenerative diseases such as Alzheimer's or Parkinson's disease.

The use of pluripotent cells stimulated to develop specialist cells ought to enable an inexhaustible source of cells and tissue to exist to combat these diseases.

Moreover, recourse to the so-called nuclear transfer technique within a sexual cell[15] is an interesting method which could alleviate the difficulties associated with the rejection of cells introduced into the organism and which are encountered during the practice of traditional cell therapy.

This technique consists of enucleating an ovocyte and introducing the nucleus of a non-germ cell into that cell[16]. The cell which is fused in this way, as well as cells deriving from it, have the potential to give rise to a living creature: these cells are therefore totipotent[17]. These cells will give rise in their turn to a blastocyst, from which cells can be isolated from the internal mass and reproduced in a culture: the cells obtained in this way will also be embryonic stem cells.

Recourse to this “therapeutic cloning” methodology has the great advantage of overcoming the problem of incompatibility in the acceptance of organs by certain patients. They will not, indeed, be faced with difficulties of this type insofar as the cells injected into them will originate, from the very outset, from their own organism.

B. Legal overview

Depending on the technique used, the legal solution will evidently differ having regard to patent law.

Moreover it should firstly be pointed out, in accordance with Recital 14 that the directive could not be interpreted as running counter to national, European and international laws laying down any limitations or prohibitions or guaranteeing control of research and the use and marketing of its results. In other words, before wondering whether a given process or product is patentable, it should firstly be checked whether a given product obtained or technique used is authorised under relevant laws and under what conditions.

As far as patent law is concerned, the sampling of multipotent cells from an adult does not seem to pose major difficulties. Any technique or product obtained will, subject to the limitations set out in Article 5(1) (non-appropriation of the human body as such), be protected by a patent if it fulfils patentability conditions.

Similarly, if the technique consisting of sampling tissue from a dead foetus is authorised by relevant laws governing ethics and research, it ought to be patentable.

On the other hand, the question of creating and using embryonic stem cells is a considerably more difficult one.

A distinction needs to be made from the outset between the mere use of embryos and the creation of embryos for research purposes.

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[15] A technique termed SCNT: Somatic Cell Nuclear Transfer.

[16] That is, any cell other than reproductive ones.

[17] There is currently no technique whereby these cells can be isolated and made to reproduce in a culture.

Under Article 6(2c) of the directive, the use of human embryos for industrial or commercial purposes is not patentable.

Recital 42 of the directive states:

"*Uses of human embryos for industrial or commercial purposes must also be excluded from patentability; [...] in any case such exclusion does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it."*

It will be the responsibility of the courts to which cases of dispute are referred to specify the scope of the terms used.

For its part, cloning is covered by Article 6(2)(a) of Directive 98/44, which lays down that:

"[...] the following, in particular, shall be considered unpatentable:
(a) processes for cloning human beings;".

This exception to patentability is based on grounds of ordre public or morality referred to in Article 6(1).

A definition of the cloning of human beings given in Recital 41, which defines it as any process, including techniques of embryo splitting, designed to create a human being with the same nuclear genetic information as another living or deceased human being.

It should be noted that the directive refers only to the question of human cloning. In fact, it was not its place to state an opinion on this question. The definitions of the embryo accordingly derive from national laws, which are particularly diverse.

The legal situation concerning the concept of embryo is completely disparate within the European Community. It does appear that the embryo is protected by law on conception in Ireland and that, accordingly, any reproduction of an embryo, whatever the stage of development, comes under the prohibition of the law.

In other countries, an embryo is only acknowledged to have a legal value as from its fourteenth day of development[18].

Reference ought to be made to the fact that the European Union's Charter of Fundamental Rights provides, in Article 3(2), for the prohibition of reproductive cloning[19]. The Convention on Human Rights and Biomedicine, signed at Oviedo on 4 April 1997[20], lays down in Article 18(2) that the creation of human embryos for research purposes is prohibited.

Nevertheless, in the light of the preparatory work for Directive 98/44, it is apparent that the European legislature wished to rule out the protection by patent of any type of cloning process.

Hence we read, concerning Article 6:

"In Paragraph 2(a), the Council deemed it more correct to use the expression 'processes for cloning human beings' than 'processes for human reproductive cloning'" [Unofficial translation][21].

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[18] For more information, see the 15th Opinion of the European Group on Ethics in Science and New Technologies of 14 November 2000, entitled "Ethical aspects of human stem cell research and use": http://.europa.eu.int/comm/european_group_ethics.

[19] *Op. cit.*, Footnote 17.

[20] http ://www.coe.fr/fr/txtjur/164fr.htm.

[21] Communication from the Commission to the European Parliament in accordance with Article 189B(2), second sub-paragraph of the EC Treaty - joint position adopted by the Council on 26 February 1998 on the proposal for a directive from the European Parliament and the Council on the legal protection of biotechnological inventions. SEC(1998) 360 final - 95/0350(COD), p. 7.

To have an exhaustive view of the situation, it should finally be pointed out that the directive excludes from patentability processes, the use of which offend against human dignity, such as processes to produce chimeras from germ cells or totipotent cells of humans and animals[22].

Here too, it will be the responsibility of the courts to which cases of dispute are referred to specify the scope of the exclusions envisaged.

Conclusion

In conclusion, forthcoming (technical and legal) developments in the field of human stem cells ought to enable us to have a clearer view of the legal situation applicable.

On 18 October 2000, the European Group on Ethics was commissioned by President Prodi to study the ethical aspect of the patentability of inventions involving human stem cells[23].

Furthermore, pursuant to Article 16(c) of Directive 98/44, the Commission will provide the European Parliament and the Council, in the course of 2001, with a report on the development and implications of patent law in the field of biotechnology and genetic engineering.

Directive 98/44 of the European Parliament of 6 July 1998 on the legal protection of biotechnological inventions was adopted after long and constructive discussions both within the European Parliament and the Council: it has enabled balanced solutions to be drawn up in relation to the patentability of living material.

It is in the European Community's interest to watch carefully any changes which might take place in the biotechnology field.

[22] Recital 38.

[23] See page 14 of the aforementioned opinion. It is worthwhile pointing out that, under the terms of Article 7 of the Directive, the European Group on Ethics evaluates all ethical aspects associated with biotechnology. Moreover, Recital 44 adds that that Group may be consulted only where biotechnology is to be evaluated at the level of basic ethical principles, including where it is consulted on patent law.

DIRECTIVE 98/44/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 July 1998

On the legal protection of biotechnological inventions

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DIRECTIVE 98/44/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 July 1998

on the legal protection of biotechnological inventions

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 100a thereof,

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

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

Acting in accordance with the procedure laid down in Article 189b of the Treaty [3],

(1) Whereas biotechnology and genetic engineering are playing an increasingly important role in a broad range of industries and the protection of biotechnological inventions will certainly be of fundamental importance for the Community's industrial development;

(2) Whereas, in particular in the field of genetic engineering, research and development require a considerable amount of high-risk investment and therefore only adequate legal protection can make them profitable;

(3) Whereas effective and harmonised protection throughout the Member States is essential in order to maintain and encourage investment in the field of biotechnology;

(4) Whereas following the European Parliament's rejection of the joint text, approved by the Conciliation Committee, for a European Parliament and Council Directive on the legal protection of biotechnological inventions [4], the European Parliament and the Council have determined that the legal protection of biotechnological inventions requires clarification;

(5) Whereas differences exist in the legal protection of biotechnological inventions offered by the laws and practices of the different Member States; whereas such differences could create barriers to trade and hence impede the proper functioning of the internal market;

(6) Whereas such differences could well become greater as Member States adopt new and different legislation and administrative practices, or whereas national case-law interpreting such legislation develops differently;

(7) Whereas uncoordinated development of national laws on the legal protection of biotechnological inventions in the Community could lead to further disincentives to trade, to the detriment of the industrial development of such inventions and of the smooth operation of the internal market;

(8) Whereas legal protection of biotechnological inventions does not necessitate the creation of a separate body of law in place of the rules of national patent law; whereas the rules of national patent law remain the essential basis for the legal protection of biotechnological inventions given that they must be adapted or added to in certain specific respects in order to take adequate account of technological developments involving biological material which also fulfil the requirements for patentability;

(9) Whereas in certain cases, such as the exclusion from patentability of plant and animal varieties and of essentially biological processes for the production of plants and animals, certain concepts

[1] OJ C 296, 8.10.1996, p. 4 and OJ C 311, 11.10.1997, p. 12.
[2] OJ C 295, 7.10.1996, p. 11.
[3] Opinion of the European Parliament of 16 July 1997 (OJ C 286, 22.9.1997, p. 87). Council Common Position of 26 February 1998 (OJ C 110, 8.4.1998, p. 17) and Decision of the European Parliament of 12 May 1998 (OJ C 167, 1.6.1998). Council Decision of 16 June 1998.
[4] OJ C 68, 20.3.1995, p. 26.

in national laws based upon international patent and plant variety conventions have created uncertainty regarding the protection of biotechnological and certain microbiological inventions; whereas harmonisation is necessary to clarify the said uncertainty;

(10) Whereas regard should be had to the potential of the development of biotechnology for the environment and in particular the utility of this technology for the development of methods of cultivation which are less polluting and more economical in their use of ground; whereas the patent system should be used to encourage research into, and the application of, such processes;

(11) Whereas the development of biotechnology is important to developing countries, both in the field of health and combating major epidemics and endemic diseases and in that of combating hunger in the world; whereas the patent system should likewise be used to encourage research in these fields; whereas international procedures for the dissemination of such technology in the Third World and to the benefit of the population groups concerned should be promoted;

(12) Whereas the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) [1] signed by the European Community and the Member States, has entered into force and provides that patent protection must be guaranteed for products and processes in all areas of technology;

(13) Whereas the Community's legal framework for the protection of biotechnological inventions can be limited to laying down certain principles as they apply to the patentability of biological material as such, such principles being intended in particular to determine the difference between inventions and discoveries with regard to the patentability of certain elements of human origin, to the scope of protection conferred by a patent on a biotechnological invention, to the right to use a deposit mechanism in addition to written descriptions and lastly to the option of obtaining non-exclusive compulsory licences in respect of interdependence between plant varieties and inventions, and conversely;

(14) Whereas a patent for invention does not authorise the holder to implement that invention, but merely entitles him to prohibit third parties from exploiting it for industrial and commercial purposes; whereas, consequently, substantive patent law cannot serve to replace or render superfluous national, European or international law which may impose restrictions or prohibitions or which concerns the monitoring of research and of the use or commercialisation of its results, notably from the point of view of the requirements of public health, safety, environmental protection, animal welfare, the preservation of genetic diversity and compliance with certain ethical standards;

(15) Whereas no prohibition or exclusion exists in national or European patent law (Munich Convention) which precludes *a priori* the patentability of biological matter;

(16) Whereas patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person; whereas it is important to assert the principle that the human body, at any stage in its formation or development, including germ cells, and the simple discovery of one of its elements or one of its products, including the sequence or partial sequence of a human gene, cannot be patented; whereas these principles are in line with the criteria of patentability proper to patent law, whereby a mere discovery cannot be patented;

(17) Whereas significant progress in the treatment of diseases has already been made thanks to the existence of medicinal products derived from elements isolated from the human body and/or otherwise produced, such medicinal products resulting from technical processes aimed at obtaining elements similar in structure to those existing naturally in the human body and whereas, consequently, research aimed at obtaining and isolating such elements valuable to medicinal production should be encouraged by means of the patent system;

(18) Whereas, since the patent system provides insufficient incentive for encouraging research into and production of biotechnological medicines which are needed to combat rare or 'orphan' diseases, the Community and the Member States have a duty to respond adequately to this problem;

[1] OJ L 336, 23.12.1994, p. 213.

(19) Whereas account has been taken of Opinion No 8 of the Group of Advisers on the Ethical Implications of Biotechnology to the European Commission;

(20) Whereas, therefore, it should be made clear that an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, is not excluded from patentability, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to the human body and its elements in their natural environment;

(21) Whereas such an element isolated from the human body or otherwise produced is not excluded from patentability since it is, for example, the result of technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself;

(22) Whereas the discussion on the patentability of sequences or partial sequences of genes is controversial; whereas, according to this Directive, the granting of a patent for inventions which concern such sequences or partial sequences should be subject to the same criteria of patentability as in all other areas of technology: novelty, inventive step and industrial application; whereas the industrial application of a sequence or partial sequence must be disclosed in the patent application as filed;

(23) Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention;

(24) Whereas, in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs;

(25) Whereas, for the purposes of interpreting rights conferred by a patent, when sequences overlap only in parts which are not essential to the invention, each sequence will be considered as an independent sequence in patent law terms;

(26) Whereas if an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law;

(27) Whereas if an invention is based on biological material of plant or animal origin or if it uses such material, the patent application should, where appropriate, include information on the geographical origin of such material, if known; whereas this is without prejudice to the processing of patent applications or the validity of rights arising from granted patents;

(28) Whereas this Directive does not in any way affect the basis of current patent law, according to which a patent may be granted for any new application of a patented product;

(29) Whereas this Directive is without prejudice to the exclusion of plant and animal varieties from patentability; whereas on the other hand inventions which concern plants or animals are patentable provided that the application of the invention is not technically confined to a single plant or animal variety;

(30) Whereas the concept 'plant variety' is defined by the legislation protecting new varieties, pursuant to which a variety is defined by its whole genome and therefore possesses individuality and is clearly distinguishable from other varieties;

(31) Whereas a plant grouping which is characterised by a particular gene (and not its whole genome) is not covered by the protection of new varieties and is therefore not excluded from patentability even if it comprises new varieties of plants;

(32) Whereas, however, if an invention consists only in genetically modifying a particular plant variety, and if a new plant variety is bred, it will still be excluded from patentability even if the genetic modification is the result not of an essentially biological process but of a biotechnological process;

(33) Whereas it is necessary to define for the purposes of this Directive when a process for the breeding of plants and animals is essentially biological;

(34) Whereas this Directive shall be without prejudice to concepts of invention and discovery, as developed by national, European or international patent law;

(35) Whereas this Directive shall be without prejudice to the provisions of national patent law whereby processes for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body are excluded from patentability;

(36) Whereas the TRIPs Agreement provides for the possibility that members of the World Trade Organisation may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law;

(37) Whereas the principle whereby inventions must be excluded from patentability where their commercial exploitation offends against *ordre public* or morality must also be stressed in this Directive;

(38) Whereas the operative part of this Directive should also include an illustrative list of inventions excluded from patentability so as to provide national courts and patent offices with a general guide to interpreting the reference to *ordre public* and morality; whereas this list obviously cannot presume to be exhaustive; whereas processes, the use of which offend against human dignity, such as processes to produce chimeras from germ cells or totipotent cells of humans and animals, are obviously also excluded from patentability;

(39) Whereas *ordre public* and morality correspond in particular to ethical or moral principles recognised in a Member State, respect for which is particularly important in the field of biotechnology in view of the potential scope of inventions in this field and their inherent relationship to living matter; whereas such ethical or moral principles supplement the standard legal examinations under patent law regardless of the technical field of the invention;

(40) Whereas there is a consensus within the Community that interventions in the human germ line and the cloning of human beings offends against *ordre public* and morality; whereas it is therefore important to exclude unequivocally from patentability processes for modifying the germ line genetic identity of human beings and processes for cloning human beings;

(41) Whereas a process for cloning human beings may be defined as any process, including techniques of embryo splitting, designed to create a human being with the same nuclear genetic information as another living or deceased human being;

(42) Whereas, moreover, uses of human embryos for industrial or commercial purposes must also be excluded from patentability; whereas in any case such exclusion does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it;

(43) Whereas pursuant to Article F(2) of the Treaty on European Union, the Union is to respect fundamental rights, as guaranteed by the European Convention for the Protection of Human Rights and Fundamental Freedoms signed in Rome on 4 November 1950 and as they result from the constitutional traditions common to the Member States, as general principles of Community law;

(44) Whereas the Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology; whereas it should be pointed out in this connection that that Group may be consulted only where biotechnology is to be evaluated at the level of basic ethical principles, including where it is consulted on patent law;

(45) Whereas processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit in terms of research, prevention, diagnosis or therapy to man or animal, and also animals resulting from such processes, must be excluded from patentability;

(46) Whereas, in view of the fact that the function of a patent is to reward the inventor for his creative efforts by granting an exclusive but time-bound right, and thereby encourage inventive activities,

the holder of the patent should be entitled to prohibit the use of patented self-reproducing material in situations analogous to those where it would be permitted to prohibit the use of patented, non-self-reproducing products, that is to say the production of the patented product itself;

(47) Whereas it is necessary to provide for a first derogation from the rights of the holder of the patent when the propagating material incorporating the protected invention is sold to a farmer for farming purposes by the holder of the patent or with his consent; whereas that initial derogation must authorise the farmer to use the product of his harvest for further multiplication or propagation on his own farm; whereas the extent and the conditions of that derogation must be limited in accordance with the extent and conditions set out in Council Regulation (EC) No 2100/94 of 27 July 1994 on Community plant variety rights [1];

(48) Whereas only the fee envisaged under Community law relating to plant variety rights as a condition for applying the derogation from Community plant variety rights can be required of the farmer;

(49) Whereas, however, the holder of the patent may defend his rights against a farmer abusing the derogation or against a breeder who has developed a plant variety incorporating the protected invention if the latter fails to adhere to his commitments;

(50) Whereas a second derogation from the rights of the holder of the patent must authorise the farmer to use protected livestock for agricultural purposes;

(51) Whereas the extent and the conditions of that second derogation must be determined by national laws, regulations and practices, since there is no Community legislation on animal variety rights;

(52) Whereas, in the field of exploitation of new plant characteristics resulting from genetic engineering, guaranteed access must, on payment of a fee, be granted in the form of a compulsory licence where, in relation to the genus or species concerned, the plant variety represents significant technical progress of considerable economic interest compared to the invention claimed in the patent;

(53) Whereas, in the field of the use of new plant characteristics resulting from new plant varieties in genetic engineering, guaranteed access must, on payment of a fee, be granted in the form of a compulsory licence where the invention represents significant technical progress of considerable economic interest;

(54) Whereas Article 34 of the TRIPs Agreement contains detailed provisions on the burden of proof which is binding on all Member States; whereas, therefore, a provision in this Directive is not necessary;

(55) Whereas following Decision 93/626/EEC [2] the Community is party to the Convention on Biological Diversity of 5 June 1992; whereas, in this regard, Member States must give particular weight to Article 3 and Article 8(j), the second sentence of Article 16(2) and Article 16(5) of the Convention when bringing into force the laws, regulations and administrative provisions necessary to comply with this Directive;

(56) Whereas the Third Conference of the Parties to the Biodiversity Convention, which took place in November 1996, noted in Decision III/17 that 'further work is required to help develop a common appreciation of the relationship between intellectual property rights and the relevant provisions of the TRIPs Agreement and the Convention on Biological Diversity, in particular on issues relating to technology transfer and conservation and sustainable use of biological diversity and the fair and equitable sharing of benefits arising out of the use of genetic resources, including the protection of knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity',

[1] OJ L 227, 1.9.1994, p. 1. Regulation as amended by Regulation (EC) No 2506/95 (OJ L 258, 28.10.1995, p. 3).

[2] OJ L 309, 31.12.1993, p. 1.

HAVE ADOPTED THIS DIRECTIVE:

CHAPTER I

Patentability

Article 1

1. Member States shall protect biotechnological inventions under national patent law. They shall, if necessary, adjust their national patent law to take account of the provisions of this Directive.

2. This Directive shall be without prejudice to the obligations of the Member States pursuant to international agreements, and in particular the TRIPs Agreement and the Convention on Biological Diversity.

Article 2

1. For the purposes of this Directive,

(a) 'biological material' means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system;

(b) 'microbiological process' means any process involving or performed upon or resulting in microbiological material.

2. A process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.

3. The concept of 'plant variety' is defined by Article 5 of Regulation (EC) No 2100/94.

Article 3

1. For the purposes of this Directive, inventions which are new, which involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.

2. Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.

Article 4

1. The following shall not be patentable:

(a) plant and animal varieties;

(b) essentially biological processes for the production of plants or animals.

2. Inventions which concern plants or animals shall be patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety.

3. Paragraph 1(b) shall be without prejudice to the patentability of inventions which concern a microbiological or other technical process or a product obtained by means of such a process.

Article 5

1. The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

3. The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.

Article 6

1. Inventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.

2. On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:

(a) processes for cloning human beings;

(b) processes for modifying the germ line genetic identity of human beings;

(c) uses of human embryos for industrial or commercial purposes;

(d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

Article 7

The Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology.

CHAPTER II

Scope of protection

Article 8

1. The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention shall extend to any biological material derived from that biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.

2. The protection conferred by a patent on a process that enables a biological material to be produced possessing specific characteristics as a result of the invention shall extend to biological material directly obtained through that process and to any other biological material derived from the directly obtained biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.

Article 9

The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product in incorporated and in which the genetic information is contained and performs its function.

Article 10

The protection referred to in Articles 8 and 9 shall not extend to biological material obtained from the propagation or multiplication of biological material placed on the market in the territory of a Member State by the holder of the patent or with his consent, where the multiplication or propagation necessarily results from the application for which the biological material was marketed, provided that the material obtained is not subsequently used for other propagation or multiplication.

Article 11

1. By way of derogation from Articles 8 and 9, the sale or other form of commercialisation of plant propagating material to a farmer by the holder of the patent or with his consent for agricultural use implies authorisation for the farmer to use the product of his harvest for propagation or multiplication by him on his own farm, the extent and conditions of this derogation corresponding to those under Article 14 of Regulation (EC) No 2100/94.

2. By way of derogation from Articles 8 and 9, the sale or any other form of commercialisation of breeding stock or other animal reproductive material to a farmer by the holder of the patent or with his consent implies authorisation for the farmer to use the protected livestock for an agricultural purpose. This includes making the animal or other animal reproductive material available for the purposes of pursuing his agricultural activity but not sale within the framework or for the purpose of a commercial reproduction activity.

3. The extent and the conditions of the derogation provided for in paragraph 2 shall be determined by national laws, regulations and practices.

CHAPTER III

Compulsory cross-licensing

Article 12

1. Where a breeder cannot acquire or exploit a plant variety right without infringing a prior patent, he may apply for a compulsory licence for non-exclusive use of the invention protected by the patent inasmuch as the licence is necessary for the exploitation of the plant variety to be protected, subject to payment of an appropriate royalty. Member States shall provide that, where such a licence is granted, the holder of the patent will be entitled to a cross-licence on reasonable terms to use the protected variety.

2. Where the holder of a patent concerning a biotechnological invention cannot exploit it without infringing a prior plant variety right, he may apply for a compulsory licence for non-exclusive use of the plant variety protected by that right, subject to payment of an appropriate royalty. Member States shall provide that, where such a licence is granted, the holder of the variety right will be entitled to a cross-licence on reasonable terms to use the protected invention.

3. Applicants for the licences referred to in paragraphs 1 and 2 must demonstrate that:

(a) they have applied unsuccessfully to the holder of the patent or of the plant variety right to obtain a contractual licence;

(b) the plant variety or the invention constitutes significant technical progress of considerable economic interest compared with the invention claimed in the patent or the protected plant variety.

4. Each Member State shall designate the authority or authorities responsible for granting the licence. Where a licence for a plant variety can be granted only by the Community Plant Variety Office, Article 29 of Regulation (EC) No 2100/94 shall apply.

CHAPTER IV

Deposit, access and re-deposit of a biological material

Article 13

1. Where an invention involves the use of or concerns biological material which is not available to the public and which cannot be described in a patent application in such a manner as to enable the invention to be reproduced by a person skilled in the art, the description shall be considered inadequate for the purposes of patent law unless:

(a) the biological material has been deposited no later than the date on which the patent application was filed with a recognised depositary institution. At least the international depositary authorities which acquired this status by virtue of Article 7 of the Budapest Treaty of 28 April 1977 on the international recognition of the deposit of micro-organisms for the purposes of patent procedure, hereinafter referred to as the 'Budapest Treaty', shall be recognised;

(b) the application as filed contains such relevant information as is available to the applicant on the characteristics of the biological material deposited;

(c) the patent application states the name of the depository institution and the accession number.

2. Access to the deposited biological material shall be provided through the supply of a sample:

(a) up to the first publication of the patent application, only to those persons who are authorised under national patent law;

(b) between the first publication of the application and the granting of the patent, to anyone requesting it or, if the applicant so requests, only to an independent expert;

(c) after the patent has been granted, and notwithstanding revocation or cancellation of the patent, to anyone requesting it.

3. The sample shall be supplied only if the person requesting it undertakes, for the term during which the patent is in force:

(a) not to make it or any material derived from it available to third parties; and

(b) not to use it or any material derived from it except for experimental purposes, unless the applicant for or proprietor of the patent, as applicable, expressly waives such an undertaking.

4. At the applicant's request, where an application is refused or withdrawn, access to the deposited material shall be limited to an independent expert for 20 years from the date on which the patent application was filed. In that case, paragraph 3 shall apply.

5. The applicant's requests referred to in point (b) of paragraph 2 and in paragraph 4 may only be made up to the date on which the technical preparations for publishing the patent application are deemed to have been completed.

Article 14

1. If the biological material deposited in accordance with Article 13 ceases to be available from the recognised depositary institution, a new deposit of the material shall be permitted on the same terms as those laid down in the Budapest Treaty.

2. Any new deposit shall be accompanied by a statement signed by the depositor certifying that the newly deposited biological material is the same as that originally deposited.

CHAPTER V

Final provisions

Article 15

1. Member States shall bring into force the laws, regulations and administrative provisions necessary to comply with this Directive not later than 30 July 2000. 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. The methods of making such reference shall be laid down by Member States.

2. Member States shall communicate to the Commission the text of the provisions of national law which they adopt in the field covered by this Directive.

Article 16

The Commission shall send the European Parliament and the Council:

(a) every five years as from the date specified in Article 15(1) a report on any problems encountered with regard to the relationship between this Directive and international agreements on the protection of human rights to which the Member States have acceded;

(b) within two years of entry into force of this Directive, a report assessing the implications for basic genetic engineering research of failure to publish, or late publication of, papers on subjects which could be patentable;

(c) annually as from the date specified in Article 15(1), a report on the development and implications of patent law in the field of biotechnology and genetic engineering.

Article 17

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

Article 18

This Directive is addressed to the Member States.

Done at Brussels, 6 July 1998.

For the European Parliament	*For the Council*
The President	*The President*
J. M. GIL-ROBLES	R. EDLINGER

THE PATENTABILITY IN THE UNITED STATES

Maria C. FREIRE

Ph.D.
Chief Executive Officer
The Global Alliance for TB Drug Development
Brussels – New York

Intellectual property and access issues on stem cell technology

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Presentation during the Round Table
On "Ethical aspects of patenting inventions involving human stem cells"
Organised by the EGE on November 20, 2001 in Brussels

Intellectual Property and Access Issues on Stem Cell Technology

Summary[1] of Mrs Freire's presentation during the Round Table on "Ethical Aspects of patenting inventions involving human stem cells" organised by the EGE on November 20, 2001 in Brussels

The three main points of the presentation were as follows:

1. The United States legislation on technology transfer;

2. The National Institute of Health (NIH) research tools' guidelines and the importance of allowing scientists access to the core technologies;

3. The agreement negotiated between the NIH and WiCell, the key patent holder with the stem cell technology

1. The United States legislation on technology transfer

In the 1980s, three pieces of law were enacted in order to encourage universities to transfer the technologies that were federally funded: the *Bayh-Dole Act*, the *Stevenson-Wydler Act* and the *Federal Technology Transfer Act*. These three Acts have a direct impact on the stem cells' story.

The *Bayh-Dole Act*: The United States Congress encouraged the commercialisation of the technologies that arose from the research funded by the NIH and the Government. The idea was that garnering these technologies, patenting the intellectual property, and moving it forward for public benefit would enhance the economic development of the United States. This strategy of mammoth investment in public health is often considered to be at the origins of the creation of the biotechnology industry in the United States.

The key elements of this law were access to, and utilisation and broad distribution of these technologies. To achieve that, United States university professors were encouraged to patent. The universities, not the professors, retained the title to the patents and were encouraged to move it forward.

The *Stevenson-Wydler Act* and the *Federal Technology Transfer Act*: They are very similar. The only difference is that the *Stevenson-Wydler Act* relates to Government agencies, such as the NIH, the Food and Drug Administration, or the Center for Disease Control. Researchers working for these institutions were also encouraged to capture technologies. Again, the Government agencies, not the researchers, own the patent rights and are then charged for moving it forward.

[1] Summary prepared by the Secretariat of the EGE (European Group on Ethics in Sciences and New Technologies to the European Commission)

As a result of this policy, the NIH became good at protecting the intellectual property and at garnering an entrepreneurial infrastructure. But sometime, the NIH forgot perhaps that its first most important mission was the funding of research for the furtherance of public health.

2. The NIH research tools' guidelines and the importance of allowing scientists access to the core technologies

Another consequence of this policy was that the NIH found itself in a problematic situation: tools that have been developed using NIH technology where not broadly accessible by researchers in other universities. That was the case for the stem cells technology or for the oncomouse - the universities could not access this oncomouse for research purposes without signing agreements, even though the United States Congress invested in the project. And when scientists are not able to use basic tools for research, the whole scientific enterprise suffers.

This is why the NIH decided to come up with a set of rules and guidelines for all its grantees. These rules and guidelines state that the *Bayh-Dole Act*, which allowed for the patenting of technologies, but also required broad utilisation and the furtherance of research, should be appropriately implemented. They also ask NIH scientists developing research tools to disseminate them broadly to their colleagues and the scientific community.

Additionally, in order to minimise administrative burdens - people were taking six to eight months to transfer a basic cell line from one laboratory to the other - the NIH, along with colleagues at the universities, came up with a one page agreement according to which access to technologies was given for research but not therapeutic purposes. Under this one page agreement, scientists are not allowed to use or insert any of this technology or material into humans, and have to respect the appropriate terms and conditions for doing basic research.

It is worth mentioning these guidelines with regards to the stem cells because, in many instances, they represent a prime research tool – Mrs Freire insisted on the fact that she was saying that with a great deal of respect, understanding where these cells came from. Therefore, following President Bush's decision on the use of stem cells in August 2001, one understands that the NIH had to ensure that the scientists could access them, in accordance with the NIH core principles and mission.

3. The agreement negotiated between the NIH and WiCEll, the key patent holder with the stem cell technology

Before going into the details of the agreement giving NIH scientists access to the cells, a few points need to be clarified regarding the existing patents on stem cells, more precisely regarding James Thomson' s patent.

- Firstly, James Thomson's research was funded by the NIH only for his work on primates, but not for his work on humans, because the United States has a ban on federally funded research having to do with human stem cells.

James Thomson, operating under the rules of the *Bayh-Dole Act*, filed a first patent application on his work on primates through his university - in the case of the Wisconsin University, it is done through the Wisconsin Alumni Research Foundation (WARF) that owns the patents. A first patent was issued in the late 1990s with claims to primates. A second patent that was issued in 2001 is a continuation of the first one. One could argue that humans are primates. However, in an interesting move, the US Patent & Trademark Office issued a second patent, identical to the first one, except that it says humans rather than primates. There was no NIH funding in relation to the patent that related to human stem cells. But by virtue of the fact that the NIH funded the first patent, it has some rights to the stem cells technology.

- Secondly, to further clarify the history, the stem cells research done on humans was funded by a private company called Geron. The Geron facilities, in the University of Wisconsin, were completely separated and no Federal funds were used to study the human stem cells. Because the company had funded the research, it had the rights to some of the developed technology - this is fairly standard both in European and American agreements. That is why the Wisconsin Alumni Foundation gave Geron exclusive rights to six cell types. However, Wisconsin reserved the right for research purposes and narrowed what they granted back to Geron to six cell types, which happened to coincide with the most important medical applications...

- Finally, the various players need to be clarified:
    - James Thomson did the research;
    - the Wisconsin University owns the intellectual property through the WARF;
    - the Wisconsin University created a subsidiary called WiCell -Wisconsin Cells Company- in order to handle all the requests for stem cells.
      WiCell now has the rights for the scaling up and distribution of the stem cells.

The issue of accessing the stem cells became crucial after President Bush announced his decision on stem cells on August 9th 2001. He said very clearly that only the 60 cell lines or so that were identified at that date could be used for research using federal funds. Consequently, the NIH had to come up with an agreement with WARF, the key holder of the stem cells patent, or more precisely with WiCell, because they are the holders of the intellectual property, and more importantly, of the cell lines. An important thing to realise is that even if researchers can get access to the intellectual property or to the patents through a licence agreement, they do not necessarily get access to the tangible property - the actual cells. And in this case, no researcher could make the cells, because that was part of the presidential directive. So they had to access the cells themselves. Thus the NIH had to craft an agreement that not only allowed for the use of intellectual property, but also for the receiving of the cells that had already been created, so no more embryos would be destroyed.

Mrs Maria Freire, on behalf of the Public Health System (which includes the NIH, the Center for Disease Control and the Food and Drug Administration), negotiated this agreement with the Wisconsin University people. They knew and understood that the NIH had some rights to the stem cells technology by virtue of the fact that the NIH had funded the primate technology.

So, unlike the case of the oncomouse, where the NIH had to prevail on the good will of the company, in the case of the stem cells, the NIH had some residual rights that Wisconsin acknowledged and took into account during the negotiations. The anatomy and the critical features of the resulting agreement are as follows.

- Firstly, and most importantly, the commercial uses were separated from the research uses. This separation ensured that NIH scientists could access these tools for no commercial purposes, thus allowing basic research to move forward.

- Secondly, the NIH agreed that the intellectual property remained with the inventors, Wisconsin. But the NIH did not allow "reach-through rights", in accordance with its long established position against this kind of rights. Reach-through are rights whereby the owner of a certain material retains the ownership on any invention developed with this material. In the NIH / Wisconsin agreement, the cells are considered as research tools, and inventors using them retain the rights to their own inventions, unless the cells are part of the final invention.

- Thirdly, the NIH noticed that some of the already identified stem cell lines around the world fall within the WARF patent. Consequently, the importation of these stem cells into the United States would in fact infringe this patent. Wisconsin agreed not to consider the importation of these cells by the NIH researchers as a violation of their patent rights. Thus, NIH researchers can work with any of the 60 cell lines that have been identified without fearing patent infringement.

- Finally, Wisconsin agree to extend the terms of the agreement to any recipient of NIH funding that wishes to have the same terms and conditions, thus allowing a larger part of the scientific community to research on the stem cells.

The practical details of the agreement are as follows:

- The cells can be transferred through a Material Transfer Agreement, which a one-page agreement allowing the cells to be used for non-commercial purposes (if people want to use the cells for commercial purposes, they have to sign a different kind of agreement with Wisconsin);

- The NIH researchers cannot redistribute the cells. If somebody else wants to access the cells, they can go to Wisconsin and get them directly;

- The cells will only be used as provided by law;

- NIH researchers are only charged a $ 5000 fee, which represents the cost of making and maintaining the cells. There are no royalties or additional costs.

The *quid pro quo* was that the NIH agreed to acknowledge WiCell, and acknowledge the sources of these cells in its publications (that is standard procedure within the field of scientific research anyway). Additionally, NIH researchers have to send a yearly notification saying that they are using the cells in accordance with the law (it is not a NIH standard practice, but the NIH agreed to send such a notification). Finally, the NIH agreed not to give any other party that has stem cells better terms and conditions than the ones granted to Wisconsin. So the NIH is using Wisconsin as the threshold. If better terms and conditions are given to any other providers of cells, the NIH has to go back to Wisconsin and grant the same.

In conclusion, the situation today is as follows: The NIH negotiators are going to the other providers of stem cells and crafting similar agreements with them. The scientists are able to access the cells. And hopefully, the science can continue.

THE WISCONSIN ALUMNI RESEARCH FOUNDATION AND GERON CORPORATION DISPUTE

Information Note

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This text has been prepared
by Brigitte Gratton, trainee within the EGE Secretariat

The Wisconsin Alumni Research Foundation and Geron Corporation Dispute

Information note[1]

Introduction

In November 1998, Dr. James Thomson (University of Wisconsin) first isolated and cultivated pluripotent human embryonic stem cells (human ES cells). His team established five unmodified human ES cell lines. Through the Wisconsin Alumni Research Foundation (WARF or the Foundation), he filed a patent on 26 June 1998, which was issued on 13 March 2001: US Patent 6,200,806.

WARF is an independent and non for-profit foundation affiliated to the University of Wisconsin. Its role consists of patenting the findings made by researchers at the University of Wisconsin. Because the University employs these researchers, intellectual property rights on their discoveries belong to the University, more specifically to the Foundation in charge of dealing with intellectual property rights. As owner of these patents, WARF is also responsible for licensing them. The Foundation owns US Patent 6,200,806 and licensed it to Geron.

Geron is a private biopharmaceutical company focused on developing and commercialising therapeutic and diagnostic products for application in oncology and regenerative medicine, and research tools for drug discovery. Geron sponsored James Thomson's research, as the US Government did not fund it because it used human embryos. In return for its funding, Geron was granted important rights under a licence agreement.

The WARF patent covers both the method of isolating human ES cells (the process) and the five unmodified stem cell lines themselves[2] (the product). It is a very broad patent, which gives WARF control over *who may work* with these five human ES cell lines*, over who may use James Thomson's process* to isolate the stem cells, and over the *purpose of the work* (research, commercialisation). At the moment, the WARF patent is only valid in the USA, but applications are pending in Europe.

[1] Author: Brigitte Gratton, trainee with the Secretariat of the EGE (1st March 2002 / 31st July 2002).

[2] The WARF patent includes: - a product claim on a purified preparation of pluripotent human ES cells; - a product claim on five unmodified human ES cell lines; - a process claim for isolation of stem cells from embryos; - a process claim for culturing of stem cells; - a process claim for inducing stem cells to differentiate in particular ways.

The access to stem cells

Since President Bush's announcement on the 9th August 2001, scientists whose research is federally funded are allowed to work with the 72 human ES cell lines already isolated. In practice however, the government does not have control over whether these ES cell lines get to researchers for the following reasons:

Since in the United States research using embryos can only be privately funded, many of these human ES cell lines are in the hands of private companies, and therefore access has to be negotiated. It is generally also true at international level.

When a patent exists (such as the WARF patent), a licence has to be negotiated. Furthermore, the grant of exclusive rights under a licence agreement may restrict access to the human ES cells and discourage research.

If the human ES cell lines match the description in the broadly worded WARF patent, their owners (public institutions or private companies) must obtain approval from the WARF before distributing them.

For all these reasons, the existence of a patent such as the WARF patent and the related licensing practices may impair freedom of research and access to healthcare.

The first licence agreement between WARF and Geron

Under a first licence agreement,[3] WARF granted to Geron *exclusive rights* to develop the unmodified stem cell lines isolated by Dr. James Thomson into six specific modified stem cell lines[4] (relating to liver, muscle, nerve, pancreas, blood, and bone cells) for commercial purpose. It means that Geron exclusively was allowed to develop and commercialise therapeutic and diagnostic products involving these six stem cell *types*.

The Foundation retained the right to distribute its unmodified stem cell *lines* to the academic research community. These stem cell lines were and are still available from WiCell Research Institute, a WARF subsidiary.[5]

[3] The first and the second licence agreements remain confidential. Informations about their contents are therefore from second hand sources.

[4] Modified/differentiated human ES cell lines can also be called human ES cell *types.* Both expressions will be used in this note.

[5] WiCell's mission is to provide scientists with the Wisconsin human ES cells.

The dispute between WARF and Geron

On the 13 August 2001, WARF filed a lawsuit against Geron, contesting the company's rights to additional human ES cell *types*. Indeed, on the 26 July 2001, Geron exercised an option contained in the first licence to claim 12 additional stem cell types. WARF argued that the option had expired a week earlier and that the use of the option could be denied at WARF discretion. At that time, there was no legal argument over Geron's rights to the six human ES cell types already licensed to Geron. However, WARF warned Geron that it could also loose its rights to them because its performance in developing therapies had been disappointing.

Additionally, WARF argued that Geron had no exclusive rights to *research products*[6] except in those cases when Geron added its own technology. This argument probably related to a dispute as to whether research products were included in the definition of therapeutic and diagnostic products. If that were the case, Geron would have had exclusive rights on research products involving the six human ES cell types as well.

The interests at stake

The motivations of WARF in filing the lawsuit were probably:

To stop Geron from taking too large a piece from the commercial interests at stake. Regarding the timing and context,[7] Geron obviously tried to secure potential profits when it exercised the option.

To be able to license the additional human ES cell types to other various companies.

To promote research and investment in stem cells research. Geron's exclusive commercial rights on 12 additional human ES cell types would have: - restrained the development of therapeutic and diagnostic products from these stem cell types; - generally discouraged other scientists from researching on WARF stem cells, as to commercialise any related inventions, they may need to obtain a sublicence from Geron.

[6] Example: using the stem cells to screen for drug compounds.

[7] President Bush's announcement a week earlier confined the federally funded research only to already isolated human ES cell lines.

The settlement of the dispute

The dispute was settled out of court. On the 9 January 2002, WARF and Geron signed a new licence that gives Geron:

- Exclusive rights to develop therapeutic and diagnostic products from three types of human ES cells (nerve, cardiac muscle and pancreas cells);

- Non-exclusive rights to develop therapeutic and diagnostic products from three further human ES cell types (blood, cartilage, and bone cells);

- Non-exclusive rights to develop research products in six human ES cell types.

Furthermore, WARF and Geron agreed to grant research rights to existing human ES cells patents and patent filings to academic and governmental researchers without royalties or fees.

Geron not only renounced the enlargement of its area of exclusivity, but also gave away exclusive commercial rights on three human ES cell types. Thus a monopoly situation on the *commercialisation of human ES cell types* owned by WARF was avoided. In addition, the new agreement clarifies the situation regarding research products. Finally, the new agreement clearly states the principle of free access to the human ES cell lines for academic researchers. It is, however, not so certain that the latter point was a real issue in the dispute.

The access to WARF stem cells

The current situation is that WARF gives NIH researchers and scientists working for non for-profit institutions access to its stem cell lines against a nominal fee, which covers expenses incurred for culturing and shipping the stem cells, but does not constitute a payment of royalties. Previously, WARF generally used to retain the right to provide such access to academic researchers when negotiating licence agreements (cf. Geron's licence). In September 2001, the Foundation signed an agreement with the NIH regarding access to its stem cell lines. Consequently, providing access against a nominal fee to academic researchers became legally binding for WARF. The principle of access without having to pay royalties is therefore clearly stated in Geron's new licence agreement and even extended to prospective inventions and future patents. On the other hand, private researchers have to negotiate access under a licence and to pay much more than a nominal fee.

Conclusion

Regarding the lawsuit, the first agreement apparently did not stop academic researchers from accessing the five unmodified human ES cell *lines*.

However, it:

- Precluded them from developing therapeutic and diagnostic products using the stem cell types subject to exclusive commercial rights;

- Discouraged them from developing research products involving the stem cell types as it was unclear whether they were subject to exclusive commercial rights;

- Discouraged them from researching on human stem cell lines as the commercialisation of their findings would have required a licence from WARF or even from Geron (the grant of such a licence could be refused at WARF and/or Geron's discretion).

The settlement reduces the number of stem cell types subject to exclusive commercial rights from six to three. In that sense, it opens the field of research. However, a true opening of the field of research relies on WARF. If WARF were to grant further exclusive commercial rights to others companies from the private sector, nothing would really change. If, from now, WARF decides to grant mainly non-exclusive commercial rights to other companies, then the field of research would be truly opened. But at least a monopoly situation where a single company has a commercial exclusivity on all WARF human stem cell types has been avoided.

Regarding the WARF patent, the Foundation holds a very extensive patent that could create a monopoly. This patent may be changeable in Court. Indeed, broad patents are more vulnerable to attack, and legal experts are not sure whether the WARF patent would survive the scrutiny of litigation. WARF is however apparently not willing to abuse its position, not only because it is in its commercial interests, but also because the foundation is attached to the public sector and promote the same values (namely the free access to research tools). Still it is in WARF's commercial interests to be able to grant more licences. The positive aspect is that WARF's licensing policy is not inconsistent with the advancement of basic research, in the sense that WARF is not seeking ownership of any new inventions that arise from using its stem cell lines, nor insisting on an option to have exclusive rights to these inventions.

THE EUROPEAN PATENT OFFICE

André REMOND

General Director, European Patent Office

Patentability of inventions using human stem cells

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Presentation during the Round Table
On “Ethical aspects of patenting inventions involving human stem cells”
Organised by the EGE on November 20, 2001 in Brussels

Patentability of inventions using human stem cells

Summary of Mr Remond's presentation during the Round Table on "Ethical aspects of patenting inventions involving human stem cells" organised by the EGE on November 20, 2001 in Brussels

I. INTRODUCTION

On 14 November 2000 the European Group on Ethics in Science and New Technologies to the European Commission (EGE) issued an opinion on human stem cell research and use.

The EGE plans to issue a second report on the specific ethical questions relating to the patenting of inventions involving human stem cells.

This document outlines the practice in the European Patent Office and identifies the specific problems the EPO faces in this area.

II. THE CURRENT SITUATION

Although there has been extensive public and political debate world-wide on the importance and appropriateness of stem cell research, the European Patent Office has so far received very few patent applications concerning stem cells of human embryos.

At the end of October 2001 documentary research identified 37 European patent applications. Most of these came from the United States. By the same date, 1102 patents had been issued in the infinitely broader field of human or non-human stem cells.

In 2000 the EPO granted the University of Edinburgh a patent for a method of selecting stem cells, including human stem cells derived from embryos (ES cells). There was opposition to this patent. The opposition procedure is currently under way, and a ruling will not be forthcoming before 2002.

The most controversial point raised by opponents concerns the use of human embryos as a source of cells. Even though the harvesting phase is not explicitly included in the patented method, it is clear that an embryo is often destroyed in order to obtain embryo stem cells. But the validity of the patent must also be examined in terms of whether the invention could be reproduced using human cells on the date when the patent was applied for (21 April 1994). In the United States two matching patents have been granted (14 and 21 November 2000).

III. TYPES OF INVENTION CONCERNED

The main categories of invention in this area are:

- cell selection and cultivation methods;
- stem cells *per se*;
- differentiated stem cells, e.g. haematopoietic stem cells;
- genetically modified stem cells;
- tissue and/or organs obtained from stem cells;
- uses of stem cells, e.g. for therapeutic purposes.

A patent application may involve one or more of these categories. Some patent applications for stem cells also include a preliminary phase to clone the embryo. This aspect will be discussed in Section VI.

IV. SITUATION WITH REGARD TO DIRECTIVE 98/44/EC ON THE LEGAL PROTECTION OF BIOTECHNICAL INVENTIONS

Although Article 5(1) of the Directive provides that "The human body, at the various stages of its formation and development ... cannot constitute patentable inventions", paragraph 2 states that "An element isolated from the human body ... may constitute a patentable invention". Recital No 21 specifies that such an element "is not excluded from patentability since it is, for example, the result of technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself."

This provision confirms the previous practice of the European Patent Office, whereby patents can be issued for methods of treating body tissues or fluids after they have been removed from the human or animal body (Guidelines for examination in the EPO, C-IV, 4.3) and for products derived from them. For example, the processing of blood and the various products of such operations can be patented.

Similarly, the patentability of cells isolated from the human body has never been at issue.

Patent applications for human stem cells, whether obtained from embryos, foetal tissue or adult cells, do not appear to present problems of patentability under Article 5 of the Directive. They are clearly elements isolated from the human body, at the various stages of its formation, which result from technical processes.

But Article 6 of the Directive must also be taken into consideration.

Article 6 of the Directive considers inventions in terms of public order and morality.

Article 6(2)(c) is of particular relevance with regard to human stem cells. It provides that uses of human embryos for industrial or commercial purposes are to be considered unpatentable. What is more, the list of inventions considered unpatentable as given in Article 6(2) is not exhaustive, so other categories of invention could also be excluded.

The following questions must be answered as a matter of the utmost importance:

- Is an invention consisting of a method applied to human cells of embryonic origin subject to the ban, even though the phases covered directly by the patent do not include the cell isolation phase directly involving the embryo?
- Are products resulting from these phases, such as modified stem cells or tissues cultivated from these cells, covered by the ban?
- Should we distinguish between cells derived from embryos, foetuses and adult human bodies?
- Should we differentiate on the basis of the fact that, in the specific case of embryonic stem cells, the method involves the deliberate destruction of an otherwise viable embryo, even though the foetuses used are the results of abortions which, whether spontaneous or artificially induced, are legal?
- What about cases where non-viable embryos are harvested using parthenogenesis?
- Can we justify the distinction made between foetuses and adults as sources of cells, for example, with regard to issues of dignity of the person or informed consent?

V. PATENTS AND COMMERCIALISATION

Some national laws on bioethics and international conventions ban the marketing of human body parts. These conventions are listed in the introduction to the Opinion of the European Group on Ethics of 14 November 2000 on ethical aspects of human stem cell research and use.

We should first ascertain whether the ban on commercialisation or profit making affects the issuing of patents for human stem cells.

In the classic case of blood products, for example, it is illegal in some countries to give blood donors any remuneration. A ban of this kind does not, however, in any way affect the issuing of patents for methods applied to donated blood and blood derivatives obtained from it. Blood derivatives are marketed, although this is sometimes restricted to State-controlled institutions.

As regards human stem cells, paragraph 2.17 of the Opinion of the European Group on Ethics argues that measures should be taken to prevent the commercialisation of embryos as well as cadaveric foetal tissue. Paragraph 2.18, however, seems to authorise the commercialisation of products obtained from human stem cells as it lays down conditions for such products to be imported and exported (subject to compliance with ethical and safety rules).

It should, moreover, be noted that products derived from human foetal tissue are already marketed within European Union Member States. For example, libraries of foetal cDNA are available on the market.

If the research in question is authorised, subject to the reservations set out in the EGE Opinion of 14 November 2000, and if the commercialisation of derived products is also permitted in the light of considerations of public order and morality, then logically it should be permitted to issue patents for techniques involving the isolation, growth and use of human stem cells, regardless of whether they are of embryonic origin.

The "morality" criterion of Article 53(a) of the European Patent Convention and of Article 6 of Directive 98/44/EC on the legal protection of biotechnical inventions applies to the exploitation of the invention and not to the issue of the patent:

"Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public *or morality... "*

According to these articles, if the commercial exploitation is not contrary to public order or morality, then a patent application must not be rejected.

VI. METHOD OF CLONING EMBRYOS FOR THE PURPOSES OF STEM CELL HARVESTING

This aspect is dealt with in paragraph 2.7 of the Opinion of the European Group on Ethics, which deals with research activities.

Some of the patent applications submitted to the European Patent Office deal with both the embryo creation method and the harvesting of human embryo stem cells.

In such cases, the patentability of the cloning phases needs to be looked into. Article 6(2)(a) of Directive No 98/44/EC stipulates that procedures for cloning human beings are not patentable.

If the patent application does not mention the source of the embryos, and if the patentability of the techniques used to obtain human embryo stem cells is authorised, then there is no reason to consider the method used to obtain the embryo.

VII. THE PROBLEM OF CONSENT

In addition, the donor's free and informed consent, an important condition in its own right, is not something that a patent office could be expected to check. Indeed, the principle of anonymous donation would make checking impossible (cf. EGE Opinion: Ethical aspects of human tissue banking, 21 July 1998).

THE EUROPEAN PATENT OFFICE

Information note

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This text has been prepared
by Agueda Ollero Montiel (EGE Secretariat)

The European Patent Office

Information note[1]

The European Patent Office (EPO) is the executive branch of the European Patent Organisation, an intergovernmental body set up under the European Patent Convention (EPC), **aiming to establish an uniform patent system in Europe**. The European Patent Organisation counts 20 memberships.

The activities of the EPO are supervised by the Organisation's Administrative Council, composed of delegates from the contracting states. The EPO started working in 1978.

The EPO grants European patents for inventions, for the contracting states to the European Patent Convention (EPC), which was signed in Munich on 5 October 1973 and entered into force on 7 October 1977. The first revision of the EPC took place in 2000 and was completed with a view to modernising the European patent system and adapting it to meet the challenges of a globalising economy.

The EPC is linked to the Patent Cooperation Treaty (PCT), an international treaty, which offers to over 100 countries a unitary and simplified filing procedure. **The PCT is administered by the World Intellectual Property Organization (WIPO)**.

The EPO provides patent protection for Europe on the basis of a single patent application and a single grant procedure. European patent applications and patents can also be extended to countries signing agreements to that effect with the European Patent Organisation.

Over 80% of the world's patents are granted by the EPO, by the Japanese Patent Office and by the United States Patent and Trademark Office. To improve efficiency in dealing with the growing number of patent applications, these three offices have been co-operating closely since 1983 on projects involving automation and database.

The EPO develops technical co-operation projects in many countries and regions of central and Eastern Europe, Africa, Latin America and Asia. **These projects, some of which carried out on behalf of the European Commission, are aimed at building up and modernising industrial property systems to bring them into line with the provisions of the TRIPS[2] Agreements**.

[1] Note prepared by Agueda Ollero Montiel (EGE Secretariat).
[2] TRIPS : Trade-Related Aspects of Intellectual Property Rights.

WORLD TRADE ORGANISATION

Thu-Lang TRAN WASESCHA

Counsellor in the Intellectual Property Division of the World Trade Organisation (WTO) in Geneva

The WTO and the TRIPS Agreement

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Presentation during the Round Table
On "Ethical aspects of patenting inventions involving human stem cells"
Organised by the EGE on November 20, 2001 in Brussels

The WTO and the TRIPS Agreement

Summary of Mrs Tran Wasescha's presentation during the Round Table On "Ethical aspects of patenting inventions involving human stem cells" Organised by the EGE on November 20, 2001 in Brussels

The WTO and the TRIPS Agreement

The first part of this presentation will address the WTO (World Trade Organisation) architecture and the place of the TRIPS (Trade-Related Aspects of Intellectual Property Rights) in the WTO structure. The second part will deal with the patent provisions of relevance to the debate of this Round Table. A brief description of the work in the TRIPS Council will be given, in particular with regard to biotechnology and in the light of the results of the Fourth Ministerial Conference in Doha in November. Finally, some comments will be offered on the "case law" regarding some concepts of relevance to the debate, such as public order or morality.

The WTO Architecture

The WTO, successor to the former GATT (which was not an intergovernmental organization but an entity formed by the Contracting Parties to the General Agreement on Tariffs and Trade of 1947) has 144 Members[1], one of the two last ones being China. Its supreme body is the Ministerial Conference, which is held every two years. Next to the Ministerial Conference is the General Council, which acts on behalf of the Ministerial Conference in the interim. Three main "pillars" form the architecture of the WTO system:

- the GATT (General Agreement on Tariffs and Trade), dealing with goods;
- the GATS (General Agreement on Trade in Services);
- and TRIPS for intellectual property.

The GATT "pillar" covers a number of agreements dealing with various areas such as agriculture. All these agreements, the GATS and the TRIPS Agreement form a "package": countries adhering to the WTO system must accept the whole "package", they cannot "pick-and-choose". Apart from these agreements forming the package, adherence to certain agreements (government procurement and civil aircraft) is not mandatory; they are referred to as "plurilateral" agreements.

Disputes arising between WTO Members are resolved through the Dispute Settlement Mechanism. It is composed of two bodies: - the Dispute Settlement Body. Rulings pronounced by this body can be appealed to a distinct organ: - the Appellate Body.

[1] Situation as of 31 March 2002.

One of the reasons for the issue of intellectual property to be brought to the former GATT was the fact that the dispute settlement system in the intellectual property conventions before and at the time of the Uruguay Round was not deemed efficient enough. More than in any other intergovernmental organizations, the WTO is essentially Member-driven. With regard to decision-making, it works mainly on the consensus principle.

General comments on intellectual property

Intellectual property is not a new area created by the WTO as some would tend to believe. It is a very long standing discipline. One of its foundations at the multilateral level is the Paris Convention for the Protection of Industrial Property, administered by the World Intellectual Property Organization in Geneva; it dates back from the end of the 19th century. This long-standing discipline was built on through constant efforts to strike a balance between various interests. As pointed out by previous speakers, there are, on one side, the interests of innovators and researchers, who seek reward for their efforts in making research into the development of new products and, on the other side, the interest of society at large to have the technology disseminated.

The TRIPS Agreement is an example of this attempt to achieve a balance; this balance can be found throughout the agreement. It is enshrined in particular in two provisions in Part I on General Provisions and Basic Principles.

Article 7 (Objectives) says that "The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations".

Another provision, Article 8 (Principles) provides that "Members may, in formulating or amending their laws and regulations, adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development, provided that such measures are consistent with the provisions of this Agreement". It furthers says that "Appropriate measures, provided that they are consistent with the provisions of this Agreement, may be needed to prevent the abuse of intellectual property rights by right holders or the resort to practices which unreasonably restrain trade or adversely affect the international transfer of technology."

Patent protection is important for Research & Development: this is worldwide recognized. It does not affect government efforts to safeguard *ordre public*, morality, public health or environment, for example in the field of biotechnology. Nothing in the TRIPS Agreement prevent Members to regulate Research & Development in the area of biotechnology, as long as it does not contravene the provisions of the Agreement. As we will see later, there are a number of provisions which allows flexibility for Members.

Finally, patent owners do not have the absolute right to do what they want with the patented invention in the country where it has been granted if certain conditions are not fulfilled (safety, environment, etc.).

The TRIPS provisions

The TRIPS Agreement contains minimum requirements. It allows Members to have more extensive protection if they want, provided it does not contravene the TRIPS Agreement. Members, like the European Communities and their members States, the United States, Switzerland, Australia or Japan as well as a number of developing countries have already adopted higher level of protection than that provided in the TRIPS Agreement (for example patent term restoration or certificate of supplementary protection, or patentability of plants). With regard to patent protection, although it provides for a minimum level of protection, this level represents a step forward in terms of protection: this is often referred to as the "Paris plus", Paris being the Paris Convention for the Protection of Industrial Property.

Subject to transitional arrangements for certain categories of Members (developing and least-developed countries) and to certain exceptions, Members are obliged to provide for protection to product and process inventions (Article 27.1). No discrimination between fields of technology is permitted; this obligation of non-discrimination is subject to certain exceptions (for example with regard to inventions relating to living material like plants).

Article 27.1 also provides the conditions for an invention to be patentable: novelty, inventive step (or non-obviousness) and industrial applicability (or utility). The TRIPS Agreement does not define these three concepts; definitions have to be found in nationals' laws, regulations and practices or in some other international treaties. The fact that national laws may determine the test for these criteria might have led to some hot debate, for example in the field of biotechnology with regard to the novelty or inventive step criteria.

As said before, the obligation to provide for patent protection is not "absolute". Again, the constant attempt to strike a balance between various interests is well reflected in Article 27.2, which gives Members the possibility to exclude from patentability inventions, "the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human life or health, animal life or health, plant life or health, or to avoid serious prejudice to the environment". This provision is relevant to the debate in this group. The wording is broad enough to cover ethical and other concerns in the field of biotechnology. This possibility of excepting certain inventions from patent protection is subject to the condition that such exclusion is not made merely because the exploitation is prohibited by a law.

Another exclusion possible concerns "diagnostic, therapeutic and surgical methods for the treatment of humans and animals" (Article 27.3(a)). Members have also the possibility to exclude from patent protection plants and animals and essentially biological processes for production of plants and animals; they have, however, the minimum obligation to grant patent protection to inventions relating to micro-organisms and non-biological processes and micro-biological processes for production of plants and animals. In the area relating to plants, Members have the obligation to protect plant varieties by patent protection, an effective sui *generis* (special) system of protection or by both. The provisions under Article 27.3(b) are subject to review since 1999. In the course of the review, a number of questions and concerns were raised, including on the patentability of living material. One feature of the "social contract" made between the inventor and society at large is, in return to an exclusive right for a limited period of time, the obligation to disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art ("enabling clause"). The enabling clause is enshrined in Article 29.1.

Disclosure performs the function of dissemination of knowledge but it also has the advantage of ensuring great transparency, allowing for example third parties to scrutinize certain patent

applications or patents, which could be rejected or cancelled for lack of novelty or of inventive step or for violating other provisions like public order or morality. Recent cases like the turmeric or neem tree ones, where third parties were enabled to challenge the protection wrongly obtained, are good examples that the patent system can perform the functions attributed to it by the legislator, and contains certain corrective mechanisms.

Patents give their owners the "negative" right to prevent others from performing certain acts without their authorization. They do not have a "blank check" for doing anything they wish (Article 28). This exclusive right lasts for a term of 20 years from the date of filing the patent application (Article 33). In certain areas, like pharmaceuticals, this term may be considerably shortened due to other legal or administrative rules for marketing approval.

Rights are not absolute; they are subject to exceptions. The TRIPS Agreement provides for limited exceptions to rights (Article 30). It does not, however, list those exceptions and leave this to national laws. Typically, exceptions are, for example private use, use for teaching purposes or non-commercial experimentation. A WTO panel ruled out, in a dispute between the EC and Canada in the field of patent protection for pharmaceuticals, that governments may allow manufacturers of generic drugs to use the patented invention for the purpose of obtaining marketing approval from public authorities; generic producers can then market their generic versions as soon as the patent expires (WT/DS114/R).

The TRIPS Agreement provides safeguards both for the patent owner and third parties. In case of other use without the authorization of the right holder (compulsory licenses, government use or dependent licenses), there are a series of conditions ensuring that these tools are not unduly used against the right holder but also against third parties, including competitors (Article 31). The flexibility available to Members was confirmed in Doha at the 4th Ministerial Conference in the context of the Ministerial Declaration on the TRIPS Agreement and Public Health.

The TRIPS Agreement does not give any definition of "invention", "*ordre public*", "morality", "plants", "animals", "micro-organisms", etc. Such definitions are mainly left to national laws. Trying to give a worldwide definition of concepts like morality or ethics would be a daunting exercise. It was interesting to note that, during the Uruguay Round, the Swiss delegation submitted a proposal whereby it mentioned violation of human dignity as a possible ground for refusing patent protection to an invention.

The discussions in the TRIPS Council

The body in charge of administering the TRIPS Agreement, the TRIPS Council, did examine certain questions of relevance to the debate in this Round Table. Questions and concerns were raised in the review exercise under Article 27.3(b) (the "biotechnology provision").

Issues raised could be grouped in the following categories:

- Issues concerning the link between the provisions of Article 27.3(b) and development;
- Technical issues relating to patent protection under Article 27.3(b);
- Technical issues relating to sui generic protection of plant varieties;
- Ethical issues related to the patentability of life-forms;
- Relationship to the conservation and sustainable use of genetic material;
- Relationship with the concepts of traditional knowledge and farmers' rights.

I will cite a few examples of issues of relevance to our debate here:

- The question of discovery versus invention;
- The lack of novelty in general; the lack of novelty of patent applications involving traditional knowledge;
- Problems raised by broad claims in certain applications and patents;
- Ethical concerns like the ownership of life-forms and commercialisation of life-forms.

While a number of delegations insisted on discussing the issues in the review under Article 27.3(b), others were of the view that certain issues would rather fall in the review under Article 71.1 (provision relating to the review of the implementation of the Agreement).

The debate before Doha in the TRIPS Council will continue. Issues relating to biotechnology will be discussed in the regular sessions of the TRIPS Council (as opposed to the Special Sessions of the TRIPS Council, which will deal with the negotiations on the establishment of a multilateral system of notification and registration of geographical indications for wines and spirits). Many of the issues debated before Doha are likely to be brought to the table again.

The Doha Ministerial Declaration (WT/MIN(01)/DEC/1) instructed the TRIPS Council, in pursuing its work programme including under the review of Article 27.3(b), the review of Article 71.1, and the work pursuant to paragraph 12 of the declaration (work related to implementation the relationship between the TRIPS Agreement and the Convention on Biological Diversity, the protection of traditional knowledge and folklore, and other new developments raised by Members under Article 71.1.

A separate declaration, focusing only on public health, was also adopted ((WT/MIN(01)/DEC/2): Members recognize that intellectual property protection is important for the development of new medicines and reaffirm commitments made in the TRIPS Agreement; they agree that the TRIPS Agreement does not and should not prevent Members from taking measures to protect public health; they reaffirm Members' right to use to the full, the TRIPS provisions which provide flexibility for this purpose and this context, and recognize that each provision must be read in the light of the object and purpose of the Agreement as expressed, in particular, in its objectives and principles.

Ministers also adopted a Decision on Implementation-Related Issues and Concerns (WT/MIN(01)/17), which says in its paragraph 13 that they agree that outstanding implementation issues be addressed in accordance with paragraph 12 of the Ministerial Declaration; some of the "outstanding implementation issues" raised concern, for example, the question of patenting of living organisms and their parts.

The GATT / WTO case law

As indicated before, the TRIPS Agreement does not give any definition of *ordre public* and morality. Defining concepts like those mentioned is not an easy task, the more so at the international level; some concepts like *ordre public* or morality are essentially linked to national perceptions. This being said, it should be noted that ethical and other concerns are not *terra incognita* in the GATT law. Article XX of the GATT 1947, often referred to as the "public order clause", reads as follows:

"Subject to the requirements that such measures are not applied in a manner which would constitute a means of arbitrary or unjustifiable discrimination between countries where the same conditions prevail, or a disguised restriction on international trade, nothing in this Agreement shall be construed to prevent the adoption or enforcement by any Member of measures:

(…)

necessary to protect human, animal or plant life or health;

(…)

This exception regarding certain concerns appears in Article 27.2 of the TRIPS Agreement. It is interesting to note that the public order or morality clause does not appear in other sections of the TRIPS Agreement; this does not, however, imply that the concerns do not exist for other categories of intellectual property rights. Most national laws on trademarks or industrial designs for example already contained clauses on public order or morality, some of them well before the Uruguay Round.

As indicated some moments ago, the dispute settlement mechanism is a GATT / WTO feature. Although the Appellate Body in the *Japan – Alcoholic Beverages* case rejected the panel's approach that "panel reports adopted by the GATT CONTRACTING PARTIES and the WTO Dispute Settlement Body constitute subsequent practice in a specific case" as the phrase "subsequent practice" is used in Article 31(3)(b) of the Vienna Convention on the Law of Treaties, the Appellate Body held that "Adopted" panels reports are an important part of the GATT acquis. They are often considered by subsequent panels. They create legitimate expectations among WTO Members, and, therefore, should be taken into account where they are relevant to any dispute. However, they are binding, except with respect to resolving the particular dispute between the parties to that dispute." (WT/DS8,10,11/AB/R). It is interesting to note that the same body commented that non-adopted panel reports had no binding effects but could nevertheless serve as "useful guidance". All these elements are interesting for the debate here. So far, there is no case before the Dispute Settlement Body regarding Article 27.2, Article 27.3(b) or Article 27 in general in relation to biotechnology[2]. Cases dealing with notions like public order or morality and which might help us to better understand the issue are under the GATT 1947, whether in the field of health under the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS) or in the field of environment. The first step in applying GATT Article XX exceptions is to identify whether the policy pursued through the measure falls within the range of policies designed to protect human, animal or plant life or health.

The second step consists in determining whether the specific requirements under Article XX (b) are met. Such an examination comprises the elements of "necessary" for paragraph (b) of that Article. In the *Thailand – Cigarettes* case (dispute between the United States and Thailand), the panel said that Article XX (b) clearly allowed contracting parties to give priority to human health over trade liberalization" (BISD 37S/200, panel report, para. 73). The conclusions of a panel, upheld by the Appellate Body, in a more recent case, the *EC - Abestos* case, went in the same direction (WT/DS135). Paragraph (b) of Article XX requires the performance of what has been commonly referred to as a "necessity test": measures must be necessary to "protect human, animal or plant life and health". The examination of what could be necessary is a crucial step in panel practice. A requirement of so-called "least-trade restrictiveness" was established to decide whether a measure was necessary under Article XX (b). One may say that there has been some evolution in the interpretation of the necessity requirement of Article XX (b); it has evolved from a least-trade restrictive approach to a less-restrictive one, supplemented with a proportionality test ("a process of weighing and balancing a series of factors"). It is noteworthy that the TRIPS public order or morality clause also uses the necessity test. As said earlier, there has not been any case yet with regard to

[2] See "update of WTO Dispute Settlement Cases" available at www.to.org

biotechnology in relation to Article 27.1, 27.2 or 27.3. One may wonder whether the "case law" regarding Article XX could not serve as guidance, including for the test of proportionality.

Final remarks

Could the TRIPS Agreement give clear-cut replies to the concerns raised in the context of the debate in this Roundtable?

- First, it should be recalled that it is a treaty containing minimum level of protection. Nothing prevents Members from granting more extensive protection if it does not contravene the TRIPS provisions.
- Second, the relevant provisions are drafted in a general way, with some flexibility (see for example the "may" provisions); they would need interpretation, which can only be given by panels.

As said earlier, the TRIPS provisions on patent appear to offer enough room for Members. Diagnostic, therapeutic and surgical methods for the treatment of humans and animals can be excluded from patent protection.

With regard to the patenting of biotechnological inventions, it is possible for Members to exclude from patent protection "inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provide that such exclusion is not made merely because the exploitation is prohibited by law." This key provision already appeared in a number of national laws and in international treaties like the European Patent Convention. After the expiration of the transition period for developing countries, there will be more laws containing such provisions. Experience will show how this type of clause is being applied in countries. To my knowledge, some laws – among them, certain having this provision well before the TRIPS Agreement was negotiated - have interpreted this type of clause so as to allow ethical considerations to be taken into account. In some countries, human - or to some extent too animal - dignity is a consideration that is being taken into account in the course of examination or challenges of patent applications or patents in some countries.

Before tackling the issue within the framework of the WTO and the TRIPS Agreement, one may wish to ask which aspect of the debate relating to the use of stem cells is strictly IP-related or is more general, i.e. linked to the general perception regarding life-forms, their use and possible abuses in the exploitation. Could and should the patent system be the only key to the problems raised?

Another point to consider is whether the existing TRIPS provisions, including the *ordre public* or morality clause, or the limited exceptions under Article 30, do not already offer the necessary safeguards and flexibility for countries.

Another important question relates to the definitions of concepts like "*ordre public*", "morality", etc.: could or should they be "crystallised" in a treaty like the TRIPS Agreement? Is this feasible?

It seems that the TRIPS provisions already offer enough flexibility to Members, who can determine these concepts in their laws, regulations and practices, according to their sensitiveness and domestic perceptions. It is hoped that on certain basic issues involving

life-forms, there will be a growing understanding on certain common denominators which might be accepted as yardsticks. However, this might take some time. In any event, it is of utmost importance that Research & Development into new therapies or drugs continue to be encouraged, that the patent system continues to play its role of incentive. Erosion of the patent system may result in pushing researchers into secrecy, thus depriving the society of the knowledge which forms part of the "social contract". On the other hand important concerns by the society, including those of ethical dimension, should be taken into consideration. Both objectives are not mutually exclusive.

THE WORLD TRADE ORGANISATION

Information note

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This text has been prepared
by Agueda Ollero Montiel (EGE Secretariat)

The World Trade Organisation

Information note[1]

The World Trade Organisation (WTO) is the only global international organisation dealing with the rules of trade between nations. The WTO came into force in 1995 and was created following Uruguay negotiations (1986-94). It is the successor of the General Agreement on Tariffs and Trade (GATT), established in 1947, in the wake of the Second World War.

The WTO has 144 membership. The decisions are made by entire membership. Their purpose is to help producers of goods and services, exporters and importers to conduct their business.

The WTO's top-level decision making body is the Ministerial Conference, which meets every two years. The last two meetings were held in Seattle in 1999 and in Qatar in 2001.

The heart of the WTO are the agreements, negotiated and signed by a large majority of the world's trading nations and ratified by their parliaments. These agreements are the legal ground-rules for international commerce. Essentially, they are contracts, guaranteeing to the member countries important trade rights. They also bind governments to keep their trade policies within agreed limits to everybody's benefit.

The General Agreements on Tariffs and Trade (GATT), revised during the 1986-1994 Uruguay Round, is now the WTO's principal rule book for trade in goods. **The Uruguay Round also created new rules namely for dealing with intellectual property.**

The WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights **(TRIPS[2])**, **which came into force on the first January 1995, is to date the most comprehensive multilateral agreement on intellectual property.**

The WTO's intellectual property agreement fixes the rules for trade and investment in ideas and creativity. The rules state how for example patents should be protected when trade is involved.

The agreement also describes the minimum rights that a patent owner must enjoy. But it also allows certain exceptions. Governments can refuse to issue a patent for an invention if they have prohibited for reasons of public order or morality (art. 27.2).

The Doha Declaration of the Fourth Ministerial Conference in November 2001 concerning in particular TRIPS and public health stresses that it is important to implement and interpret the TRIPS Agreement in a way that supports public health, by promoting both access to existing medicines and the creation of new ones. They refer to their separate declaration on this subject.

[1] Note prepared by Agueda Ollero Montiel (EGE secretariat).

[2] TRIPS: Trade-Related Aspects of Intellectual Property Rights.

This separate declaration sets out two specific tasks: The TRIPS Council commitment to address the problem that countries with too little or no pharmaceutical manufacturing capacity may face for compulsory licensing and the extension of the deadline for applying provisions on pharmaceutical patents until 1st January 2016 for the least developed countries.

WORLD INTELLECTUAL PROPERTY ORGANISATION

Nuno Pires de CARVALHO

Head, Genetic Resources,
Biotechnology and Associated Traditional Knowledge Section
Global Intellectual Property Issues Division
World Intellectual Property Organization (WIPO)

The Budapest Treaty and its Applicability to Human Stem Lines; the WIPO Approach on Ethical Issues

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Hearing of scientific experts
organised by the European Group on Ethics
in Science and New Technologies, 8 January 2002

The Budapest Treaty and its Applicability to Human Stem Lines the WIPO Approach on Ethical Issues

Summary[1] of Mr Nuno Pires de Carvalho's presentation during the Hearing of scientific experts organised by the EGE on January 8, 2002

1. In the first place, WIPO should like to thank the European Group on Ethics in Science and New Technologies for having being invited to participate in this discussion. WIPO, being the United Nations' specialised agency on intellectual property, has the main objective of promoting the protection of intellectual property throughout the world through co-operation among States and, where appropriate, in collaboration with any other international organization. In order to attain that objective, the Convention that established WIPO has assigned to it the mandatory function of promoting the development of measures designed to facilitate the efficient protection of intellectual property throughout the world and to harmonise national legislation in this field.

2. It should be clarified at the outset that WIPO's role is not to increase intellectual property protection at any cost, but to develop ways to facilitate its efficient protection. Efficient protection of intellectual property, it goes without saying, is not necessarily the same as increasing and expanding protection to areas where protection is not socially useful or necessary. This is why, despite WIPO Treaties' silence on ethical issues, it is so important for WIPO and its Member States to engage in a constructive discussion on possible social constraints on the expansion of intellectual property protection. A precise and correct identification of those constraints may indeed be a powerful tool to assist WIPO and its Member States to draw a line between efficient and inefficient intellectual property protection.

3. Before focusing on ethical matters, let me briefly take on the issue of the applicability of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure, of April 28, 1977, as amended on September 26, 1980, to inventions involving human stem cells.

4. The Budapest Treaty contains a practical solution to a basic problem generated by patent law requirements in the biotechnological field, namely the requirement that the details of an invention must be fully disclosed to the public, so as to permit a person skilled in the art to carry out the invention. In other words, the disclosure should enable the average expert with access to the appropriate facilities to reproduce the invention for him/herself. Disclosure is normally achieved by means of a written description supplemented where necessary by drawings. However, inventions involving the use of new micro-organisms present problems of disclosure in that repeatability often cannot be ensured by means of a written description alone. This has led to the industrial property offices in an increasing number of countries to either require or recommend that the written disclosure of an invention involving the use of a new micro-organism be supplemented by the deposit of the micro-organism in a recognized culture collection. The culture collection would then make the micro-organism available to the public at the appropriate stage in the patenting procedure.

[1] Summary prepared by the Secretariat of the EGE (European Group on Ethics in Sciences and New Technologies to the European Commission).

This was the practical solution adopted by the Budapest Treaty, under which certain culture collections are recognized as international depository authorities (IDAs) and that a deposit made with any one of them shall be recognized as valid for patent purposes by all the countries in which protection for the relevant invention has been sought.

5. It should be emphasized that this particular background has given rise to an agreement that is exclusively operational, rather than conceptual. In other words, the Budapest Treaty does not care about basic principles or concepts of patent law, but rather about how to handle deposits of micro-organisms for the single purpose of disclosure. For this reason, the Treaty does not even provide for a definition of "micro-organisms"; instead it contains a carefully devised definition of "deposit of a micro-organism" (Article 2(ii)) and it establishes how to grant "recognition and effect to the deposit of micro-organisms" (Article 3(1)).

6. This means that, on the one hand, Contracting States and IDAs are free to adopt their own definition of micro-organism, which, within reasonable scientific notions, may be more or less restrictive.

7. Furthermore, under Rule 3 of the Treaty, IDAs may limit their acceptance of micro-organisms, provided that the kinds accepted are indicated to WIPO's Director General. Lists of accepted micro-organisms may also be extended, provided the respective Contracting State also extends its assurances to the extended kinds of micro-organisms. Finally, under Rule 6, refusal of deposits is mandatory only

a) where assurances have not been provided to the kind of micro-organism for which a deposit is sought;

b) where the properties of the micro-organism are so exceptional that the IDA is not in a position to perform the tasks under the Treaty and the Regulations; and

c) where the deposit is received in a condition which clearly indicates that the micro-organism is missing or which precludes for scientific reasons the acceptance of the micro-organism. In other words, IDAs are not under the obligation of refusing the deposit of material where its nature may not correspond exactly to the scientific concept of a micro-organism.

8. The fact that the term "micro-organism" is not defined in the Treaty, and having in view that IDAs are not obliged to refuse the deposit of material that may not necessarily correspond to the generally accepted definition of micro-organism, leads to the conclusion that the term may be interpreted in a broad sense. In fact, IDAs in several Contracting States (such as Belgium, Canada, China, Germany, France, the United Kingdom and the United States) have stated that they accept the deposit of human cell lines under the terms of the Budapest Treaty, even though they are not micro-organisms in the strict sense of the word. Of course, given that the acceptance of specific material depends on the availability of technical means and facilities to receive, handle and store biological material, it happens that within the same Contracting State not all IDAs may be capable of accepting such deposits.

9. Having said this, I should draw your attention to the note contained in the WIPO's Guide to the Deposit of Micro-organisms under the Budapest Treaty, according to which whether an entity technically is or is not a micro-organism matters less in practice than whether deposit of that entity is necessary for the purposes of disclosure and whether an IDA will accept it. In other words, the Budapest Treaty's operational solution is already available for those countries whose patent law provides for the patentability in the field of human stem cells, having in mind that some IDAs have indeed opted for accepting the deposit of such material. However, where a country's patent law fails to provide for that protection, the possibility of depositing human stem cells with some IDAs is of no relevance for that same country.

Besides, the decision of requiring the deposit of human cells resides ultimately, as explained above, in the explicit language of patent law. Where patent law establishes that the description of stem cells shall be completed by the competent deposit, the application of the Budapest Treaty naturally comes to order. But where such a requirement is not imposed, the deposit shall not be even necessary.

10. Turning now to the WIPO's approach to ethical issues, it should be noted that, under Article 2 of the Paris Convention for the Protection of Industrial Property, Paris Union Members are obliged to accord to nationals[2] of other Union Members the same treatment as they accord to their own citizens. Unlike WTO Members, who are obliged to accord to other WTO Members' nationals the TRIPS minimum standards even where they fail to accord those same standards to their own nationals, if a Union Member does not accord some sort of rights to its own nationals, that Member is entitled to treat other Members' nationals likewise.

11. Of course, this aspect is important only to the extent that it may provide a legal argument for Paris Union Members that are not WTO Members, and which may be seeking to reduce patent protection. However, it does not explain whether WIPO Member States should be concerned in addressing ethical issues by means of patent-related legislative measures.

12. The debate – which, both in WIPO and other international *fora*, is far from being exhausted – is based on two common perceptions:

a) firstly, there are some areas of knowledge into which scientific research should not venture; speaking figuratively, there is – or there should be – a gate somewhere over which the old paradigm *nec plus ultra* is prominently displayed as a warning that wizard's apprentices should not dare to trespass;
b) secondly, given that patents are incentives to invent, patent protection should be denied in those areas beyond that gate, so that researchers and inventors should feel discouraged to trespass it[3].

13. Unfortunately, the second perception is partly mistaken. Patents, actually, are titles of private property and, therefore, only promote inventions in the private sector and only where competitive market conditions prevail. In sectors where governments do play an important role, either because of their direct intervention or as a result of the grant of public subsidies, patents have no relevance whatsoever. Internalization of costs, in those cases, is obtained through taxation mechanisms, not through prices. This means that the lack of patent protection shall not discourage either basic research or applied research by public or government-sponsored institutions, such as universities.

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[2] The concept of nationals of Paris Union countries extend, under the rule of assimilation established by Article 3 of the Paris Convention, to nationals of countries outside the Union who are domiciled or who have real and affective industrial or commercial establishments in the territory of one of the countries of the Union.

[3] Another common perception is that patents for biotechnological inventions lead to the private appropriation of life. Nothing could be more wrong. Patents cover inventions, which are practical solutions for technical problems. Patens permit the appropriation of those practical solutions, i.e., of the ideas, and not of the material that embodies the solutions or ideas. Furthermore, patent law is not about capturing solutions that have been developed by nature itself: it is about appropriating ideas created by human inventiveness which aim at solving specific, previously identified technical problems. Unfortunately, the misuse of the patent system by some entrepreneurs and the misguided interpretation of patent law by some patent offices have created the impression that patents allow investors in the biotechnological field to claim property rights in genes that those investors have merely identified and whose purpose they do not even know. Of course, it will take sometime until courts and parliaments correct those misuses, thus reestablishing public confidence in the patent system.

14. In its landmark opinion, delivered by Chief Justice Berger, in *Diamond v. Chakrabarty* (447 U.S. 303, 1980), the United States Supreme Court unequivocally subscribed to that view. Justice Berger wrote:

> "The grant or denial of patents on micro-organisms is not likely to put an end to genetic research or to its attendant risks. The large amount of research that has already occurred when no researcher had sure knowledge that patent protection would be available suggests that legislative or judicial fiat as to patentability will not deter the scientific mind from probing into the unknown any more than Canute could command the tides." (447 U.S. 303, at 317)

15. Therefore, elimination of public incentives is surely a much more powerful deterrent against unethical basic research than exclusion from patentability. It was not a coincidence that the recent debate in the United States on stem cell research focused exclusively on publicly funded research (in a nutshell, the US administration denied access to public funds for unwanted research on material the preparation of which requires the production (and the destruction) of new embryos).

16. Likewise, it is not patent protection alone that will encourage the private sector to engage in R&D in a given economic activity that is controlled by a state monopoly or on a market where barriers to entry guarantee the possibility of collusion among private entrepreneurs.

17. On the other hand, even as far as the private sector is concerned, it should be noted that patent protection is just one mechanism among others for private investors in R&D to internalize costs and appropriate gains. Patents do compete directly with trade secret protection, where knowledge is susceptible of being kept secret, and other indirect means of appropriation, such as existing barriers to entry, brand loyalty, exclusive dealership, etc.

18. Thus, to prohibit market access is much more effective in preventing the private sector from engaging in unethical research than denying access to patents – which, if commercial exploitation is prohibited, are meaningless pieces of printed paper.

19. This does not mean, however, that WIPO sees this debate as being irrelevant. Actually, as said above, WIPO cannot recommend unrestrained patentability because of its mandate to seek <u>efficient</u> intellectual property protection. The very issuance of patents represents a commitment of scarce social resources to the activities of patent offices in handling, processing and examining patent applications. Moreover, the enforcement of patents for socially undesirable, unethical inventions represents an additional engagement of resources that might otherwise be diverted to the enforcement of more useful areas of law. In many countries, on the other hand, patent offices must be subsidized because national inventors cannot afford the fees that patent offices should charge in order to cover the respective administrative costs. In those countries patents, therefore, represent a burden which society carries in exchange of the expectation of gains in inventive activity, creation of new businesses and job opportunities, transfer of technology, etc. Of course, patents for unethical inventions.

That society, in the first place, did not wish to be developed are not a burden – they are indeed a waste of social resources. For this single reason, patents for unethical inventions should be made unavailable, not so as to discourage their creation – because primarily, patents do not work like that – but in order to avoid the waste of social resources in protecting and enforcing those same unethical inventions.

20. On a different but related issue, recent scientific advances in research on human stem cells have dramatically increased the importance of looking anew to the matter of patenting therapeutic methods. With the exception of one or two countries, therapeutic methods have consistently been held non-patentable subject matter. The reason generally indicated for that legal solution is based on professional ethics – therapeutic methods have traditionally been scrutinized by peer review, not by patent offices, and the inventors' colleagues should naturally be entitled to share the inventions. Actually, the true reason for the lack of patent protection in the field of therapeutic methods (or for the immunity against patent infringement, as established in the United States a few years ago) lies somewhere else. Therapeutic methods, as well as diagnostic and surgical methods, are, with a very few exceptions, individual procedures whose success depends much more on the individual skills of doctors or surgeons than on the methods themselves. In other words, therapeutic methods are not to be mass applied (even where they are repeatedly applied), which characteristic confines their economic relevance to the extremely narrow market of the few patients of a given doctor or surgeon. Therefore, it is not necessary to patent those methods in order to appropriate them. Creative doctors and surgeons shall be paid through increased professional prestige and higher fees[4].

21. However, recent advances in biotechnology increase the importance of therapies and methods, especially as far as regenerative medicine is concerned. Both gene therapy and therapeutic transplantation tend to become standardized and repetitive procedures, and, therefore, they tend to be no longer performed individually by doctors and surgeons in their private offices, but rather become mass-used methods. Therapies in the biotechnology field, therefore, may become as economically important as the biotechnological products themselves, and thus have an economic role to perform on the market – rather than, allow me to repeat, in the offices of individual doctors and surgeons. Inventors of mass-used biotechnological therapeutic methods will no longer be able to internalize R&D costs through individual prestige and fees. If society is interested in promoting inventive activities of private companies in the field of biotechnological therapeutic methods, the time may come soon for a review of the scope of patent protection.

[4] *Mutatis mutandis* this also explains why patents are not granted for recipes, in spite of the fact that recipes are nothing else than literary expressions of chemical formula (and that, incidentally, that recipes were the subject matter of protection of the first patent law ever adopted, in the Greek colony of Sybaris, in the 6th century b.C.). Like therapeutic methods, the success of recipes depends on the individual skills of chefs, whose gains will stem from one or two additional stars in some cuisine guide, an expanded clientele, and higher prices, of course. Recipes, like therapeutic methods, do not need patent protection to be privately appropriated.

THE WORLD INTELLECTUAL PROPERTY ORGANISATION

Information note

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This text has been prepared
by Agueda Ollero Montiel (EGE Secretariat)

The World intellectual property organisation

Information note[1]

The World Intellectual Property Organization (WIPO) was created in 1974. **The WIPO is one of the 16 specialized agencies of the United Nations system of organizations with a mandate to administer intellectual property** matters recognized by the Member States of the UN.

The WIPO is the successor of the United International Bureaux for the Protection of Intellectual Property (BIRPI) created in 1893 from the union of the Paris Convention for the Protection of Industrial Property and the Berne Convention for the Protection of Literacy and Artistic Works.

The WIPO is intended to promote the use and protection of intellectual property worldwide.

The organization counts 178 memberships. Intellectual protection is divided in 2 categories: industrial property which includes inventions (patents), trademarks, industrial designs and geographic indications of source and copyright which covers literary and artistic works.

The value of the WIPO's program of work was enhanced by the entry into force of the TRIPS[2] Agreements on January 1st 1995, which opened a new concept in the protection and enforcement of intellectual property rights. Later on, on January 1st 1996 an agreement between the WIPO and the WTO provided for co-operation concerning the implementation of the TRIPS Agreement (notification of laws and regulations, legal, technical assistance and co-operation to developing countries).

The WIPO administers 23 treaties (16 on industrial property and 6 on copyright, plus the convention creating WIPO).

Under the Global Protection System Treaties, **The Budapest Treaty,** done in Budapest on April 28, 1977 and amended on September 26, 1980, establishes the international recognition of the deposit of microorganisms for the purposes of patent procedure.

[1] Note prepared by Agueda Ollero Montiel (EGE Secretariat).
[2] TRIPS : Trade-Related Aspects of Intellectual Property Rights.

POINT OF VIEW FROM AN INDUSTRIAL REPRESENTATIVE

Philippe BOUVET

Aventis Pharma S.A., Direction des Brevets

POINT OF VIEW FROM AN INDUSTRIAL REPRESENTATIVE

Are the rules for patenting drugs applicable to human stem cells?

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Hearing of scientific experts
Organised by the European Group on Ethics
In Science and New Technologies, 4 September 2001, in Brussels

Are the rules for patenting drugs applicable to human stem cells?

Summary[1] of Mr Bouvet's presentation during the hearing of scientific experts organised by the European Group on Ethics In Science and New Technologies, 4 September 2001, in Brussels

Vision of industrial property practitioners and, in particular, industry practitioners.

Outline of speech:

1. Current provisions concerning the acquisition and exercising of rights, more specifically in the pharmaceutical field;
2. Possible claims based on issued patents or patent applications;
3. Chief perceived obstacles to patentability of stem cells and the reasons why, in our view, these do not apply;
4. Conclusion and recommendations regarding the patentability of stem cells.

1. Current provisions concerning the acquisition and exercising of rights, more specifically in the pharmaceutical field

- According to Article 52 of the European Patent Convention, patentable inventions must be new, involve an inventive step and be susceptible of industrial application.

- Methods for treatment (by surgery or therapy) are not patentable in Europe, the aim being to ensure that doctors and veterinary surgeons are not prevented from carrying out their activities.

  These provisions can be found in France, in the national law of the other European countries and in the European Patent Convention.

- The situation is different in the United States, where treatment methods can be patented.

[1] Summary prepared by the Secretariat of the EGE (European Group on Ethics in Sciences and New Technologies to the European Commission).

- The following are patentable in Europe:
  - The products themselves;
  - Compositions containing those products, in particular formulations;
  - Feedstocks derived from those products;
  - The processes whereby those products are obtained.

  ⇒ The following are not patentable:

  - Treatment methods (whereas they are in the USA).

- Other provisions of the European Patent Convention concern the patentability of therapeutic use of substances, whether this concerns the first or second use. Claims of this type are difficult to interpret in France or elsewhere in Europe. In addition, their validity could be called into question, particularly in France (as happened in a Court of Cassation judgement).

- Specific provisions on applications concerning biotechnological inventions are set out in Directive 98/44/EC, which has been incorporated into the regulations implementing the Convention on the Grant of European Parents.

  They should be incorporated into national law. They have been in some instances but for the time being certain countries (France in particular) have refused to incorporate them.

- Thus isolated elements of the human body may constitute a patentable invention (Article 5(2) of the Directive). There are also specific provisions concerning the deposit of biological material (Article 13 of the Directive) which may apply in certain particular cases.

- Current European legislation concerning the exercising of patent rights:

- Patents do not confer power to take action but to prevent action.

  Applied in a pharmaceutical context, this means that irrespective of the patent, an authorisation for marketing drugs is necessary for them to be launched on the market.

- The rights granted by patents are limited: they enable well-defined actions to be prohibited. Exceptions to the banned actions can be found in the national law of various countries: patent rights do not extend to actions carried out on an experimental basis. In addition, various mandatory licences may be required by third parties:
  - For example, mandatory licences exist in cases of non-exploitation or the marketing of insufficient quantities, or even in cases where exploitation rights are discarded;
  - There are also automatic licences if this is in the interest of public health (Article L613-16);
  - There are also processing licences where a processing patent depends for its exploitation on a third-party patent (Article L613-11).

All the above provisions (experimental exemptions as well as mandatory licences) are safeguards against an exorbitant patent monopoly. They apply to "classic" drugs and can be applied to any other patented product or method, for example stem cells.

2. Possible claims based on patents issued or applied for

I have attempted to draw up a list of types of stem cell which we could consider protecting: adult stem cells, embryo stem cells, stem cells derived from therapeutic cloning or families of cells, foetal stem cells, etc.

Various recently published articles suggest to me that there is no certainty vis-à-vis stem cells which could be used subsequently for therapeutic purposes. Scientific opinion is divided as to the cell type which would eventually be used.

One of the main problems concerns the rejection of transplanted cells by the recipient.

This list shows that for each cell type, specific problems will arise in scientific terms and in terms of patents. It is difficult to gain an overall vision of the patent-related problems arising for all the stem cells envisaged.

Possible types of claim:

Product claims:

- Human cells characterised by their cell composition;
- Composition comprising human stem cells and an additive (Biocyte patent);
- Families of cells.

"Therapeutic" claims:

- Compositions comprising human stem cells to be used as medicine;
- Use of a composition comprising human stem cells to produce medicine for the treatment of a given illness.

Claims relating to production methods for stem cells:

- Enrichment or isolation methods;
- Methods to maintain these stem cells in vitro;
- Conservation methods.

A final possible type is the use of stem cells as a research tool or as a screening tool for small molecules (chemical molecules). These stem cells are used to determine whether a given component has an effect on a family of cells or a composition of stem cells.

3. Chief perceived obstacles to patentability of stem cells and the reasons why, in our view, these do not apply

I have tried to list the obstacles to the patentability of human stem cells which have been raised, and particularly those which have been discussed in the media.

- The lack of established families of cells which can be used for therapeutic purposes. This is a technical obstacle but one which has legal implications.

  According to the scientific press, one of the problems of human stem cells is that individuals may reject them. Legal implications arise in so far as the only product which could be protected would be a composition of stem cells defined e.g. by its cell composition.

- Another technical problem which could have legal implications by virtue of immune rejection is that the human stem cells could be prepared from an individual. What would be the impact of patent protection (the operation would be carried out in a hospital and it would be difficult to take action against the doctors)?

CCL: protection as a product of human stem cells seems to me to be relatively difficult.

The preparation methods for these stem cells could be patented. Under European law, claims to methods cover the products directly obtained from methods. However, it is difficult to demonstrate that method X was used to produce product Y. In general, patent protection of methods is more difficult to exercise than protection via product patents.

- Article 6(2) of the Directive is another potential obstacle (but I do not see it as such for the reasons I have mentioned):

  According to this article, the following are considered non-patentable:

  - Processes for cloning human beings;
  - Processes for modifying the germ line genetic identity of human beings;
  - Uses of human embryos for industrial or commercial purposes.

My fear (which is shared by the companies involved in this research on human stem cells) is that this article will be interpreted broadly.

- It is a feature of French case law that such provisions must be considered on a restrictive basis. Exceptions must be interpreted strictly.
- Which means that:
  - with regard to Article 6(2)(a), therapeutic cloning methods cannot be excluded on the grounds that they might give rise to reproductive cloning, for they are just one of the stages of reproductive cloning;
  - with regard to Article 6(2)(c): Isolated preparations of embryo stem cells cannot be considered as non-patentable. This article concerns trade in embryos rather than isolated cells.

4. Conclusion and recommendations regarding the patentability of stem cells

The question was: are the rules for patenting traditional medicines applicable to human cells?

My opinion is that:

– general patents law can apply to human stem cells especially since the rules for patentability are complemented by specific rules on the protection of biological materials;

– but the degree of protection which these patents afford would depend on the type of human stem cells used;

– in addition, other provisions on the protection of classic drugs apply, with the obstacles associated with the lack of protection for treatment methods in Europe (unlike the USA).

♦ We need to understand that the protection provided by patents in Europe is regarded as more limited than that provided in the USA because of the non-patentability of treatment methods and the difficulty for patent owners to enforce their rights on method patents.

♦ Further restrictions on the protection of inventions relating to stem cells would, at most, encourage firms which have invested in this field to keep their research findings secret or even to lose interest in them altogether, and therefore would have **very negative consequences for the public health care system.**

On the other hand, effective patent protection would certainly stimulate research in this field.

♦ We feel that it would be unjustified for several reasons to limit protection by incorporating ethical considerations into patent legislation:

– the patents field has its own "ethical" rules which are not found in general law;

– patents are not an operating licence;

– ethical problems may be linked to social problems and may evolve over time; clearly, it is not desirable for the protection of costly investments to be linked to such changes.

Recommendations

♦ Stem cells should be considered as patentable inventions.

♦ It should be clearly stated that Article 6(2) of the Directive does not apply to the patentability of stem cells or the methods used to prepare them.

= *ANNEX* =

AGENDA OF THE ROUND TABLE

Organised by the European Group on Ethics

"ETHICAL ASPECTS OF PATENTING INVENTIONS INVOLVING HUMAN STEM CELLS"

Tuesday 20 November 2001, Brussels

10.00	Welcome by Mrs Noëlle LENOIR, President of the European Group on Ethics
10.10	"**Preliminary results of a study on the patenting of inventions related to human stem cell research"** *Prof. Geertrui VAN OVERWALLE, Professor of Law, University of Leuven*
10.40	**"Preliminary results of a study on the ethical aspects of patenting life"** *Prof. Daniel KEVLES, Professor of History, Yale University*
11.10	**"Intellectual Property and Access Issues on Stem Cell Technology"** *Dr. Maria FREIRE, Global Alliance for TB Drug Development, USA*
11.40	**Discussion**
13.00	~~~~~~~~~~~~~~~~ LUNCH ~~~~~~~~~~~~~~~~~~
14.30	**The TRIPPS agreements** *Ms Thu-Lang TRAN WASESCHA, World Trade Organisation*
14.50	**The approach of the European Patent Office** *Mr André REMOND, Director, European Patent Office, Munich*
15.10	**"Human stem cells from blood cord"** *Prof. Eliane GLUCKMAN, Professor of Haematology, Department of Bone Marrow Graft, St Louis Hospital, Paris*
15.30	**"Cryoconservation of blood cord stem cell: perspective of a service provider"** *Marc WAETERSCHOOT and Dr Christine BRUNAUD, Cryo-Cell Europe*
15.50	**Discussion**
17.00	End of the Round Table

LIST OF THE PARTICIPANTS TO THE ROUND TABLE

Organised by the European Group on Ethics

"ETHICAL ASPECTS OF PATENTING INVENTIONS INVOLVING HUMAN STEM CELLS"

Tuesday 20 November 2001, Brussels

Speakers

Dr Christine BRUNAUD
Cryo-Cell Europe

Prof. Eliane GLUCKMAN
Department of Bone Marrow Graft,
St Louis Hospital Paris

Prof. Daniel KEVLES
Yale University

Ms Maria FREIRE
National Institute of Health, USA

Mr André REMOND
European Patent Office

Ms Thu-Lang TRAN WASESCHA
World Trade Organisation

Prof. Geertrui VAN OVERWALLE
University of Leuven

Mr Marc Jan WAETERSCHOOT
Cryo-Cell Europe

Members of the European Group on Ethics

Ms Noëlle LENOIR, President
Former Justice of the French Constitutional Court (1992-2001)

Mr Göran HERMERÉN, Vice-President,
Philosopher, Professor of Medical Ethics,
Faculty of medicine, Lund University

Ms Inez DE BEAUFORT
Professor of Health Care Ethics,
Medical Faculty of the Erasmus University, Rotterdam

Mr Rafael CAPURRO
Professor of Information Management and Information Ethics at Fachhochschule Stuttgart, Hochschule der Medien, University of Applied Sciences

Mr Yvon ENGLERT
Head of Fertility Clinic, Free University of Brussels (ULB), Professor of Medical Ethics and Deontology

Ms Anne McLAREN
Geneticist, Research Associate at Wellcome CRC Institute, Cambridge

Ms Linda NIELSEN
Professor of Law, University of Copenhagen

Mr Pere PUIGDOMÈNECH ROSELL
Research Professor, Department for Molecular Genetics, Director of Institut de Biologia Molecular de Barcelona, CSIC

Mr Stefano RODOTA
Professor of Civil Law, University of Rome, Chairman of the Italian Data Protection Authority, Chairman of the European Group of the Data Protection Authorities

Mr Günter VIRT
Professor of Theology, Institut of Catholic Moral Theology, University of Vienna

Mr Peter WHITTAKER
Biologist, Professor of Biology, Head of the Biology Department, National University of Ireland, Maynooth

Secretariat of the EGE

Ms Christiane BARDOUX

Ms Marie CHIROL

Ms Agueda OLLERO MONTIEL

Ms Marina PATRIARKA

European Commission

Ms Alexandra BITUSIKOVA, DG Research

Mr Didier BOUIS, DG Entreprise

Ms Roswitha BRAUCKMANN-JACKSON, SDT

Ms Paola DI PIETROGIACOMO, JRC

Mr Jean-Luc GAL, DG Internal Market

Mr Bruno HANSEN, DG Research

Ms Anna KARAOGLOU, DG Research

Mr Waldemar KÜTT, DG Research

Mr Antonio LACERDA DE QUEIROZ,
DG Entreprise

Ms Line MATTHIESSEN, DG Research

Ms Barbara RHODE, DG Research

Ms Carmelita STOFFELS, DG Research

European Parliament

Mr Jean-Marie DEHOUSSE
MEP

Ms Geneviève FRAISSE
MEP

Mr Robert GOEBBELS
MEP

Ms Helene HALDORF ROMERO
Assistant to MEP Lenart Sacredens

Mr Gordon LAKE
DG Research

Mr Dan LESKIEN
Adviser

Ms Emilie MAZZACURATI
Assistant to MEP Didier Rod

Mr Steve McGIFFEN
MEP

Ms Emilia MÜLLER
MEP

Mr John PURVIS
MEP

Mr Markus ROTHHAAR
Assistant to MEP Evelyne Gebhardt

Ms Mathilda ROTKIVCH
Assistant to MEP Astrid Thors

Ms Sally TAYLOR
Assistant to MEP John Purvis

Ms Astrid THORS
MEP

Ms Evelyn WALDHERR
MEP

Mr Jonathan EVANS
MEP

International Organisations

Mr Massimo CORSI
European Patent Office, Brussels Office

Ms Orio IKEBE
UNESCO, Division of Human Sciences,
Philosophy and Ethics of Science and
Technology, France

National Instances

Ms Andrea ARZ DE FALCO
Ethics Committee on Non-Human Gene
Technology, Suisse

Ms Maureen DALZIEL
Human Fertilisation Embryology Authority, United
Kingdom

Mr Frank DEMEYERE
Cabinet du Commissaire du Gouvernement
belge
adjoint au Ministre de la recherche
scientifique, Yvan Ylieff

Ms Hélène GAUMONT-PRAT
Comité Consultatif National d'Ethique, France

Mr Jean-Paul HARPES
Commission Nationale Consultative d'Ethique du
Luxembourg

Mr Gilbert HOTTOIS
Comité consultatif de bioéthique de Belgique

Ms Anne LYRRESKOV
Danish Council of Ethics

Mr Octavi QUINTANA TRIAS
Ministry of Health and Consumer Affairs, Spain

Ms Isabel SERINA
Spanish Patent and Trade Mark Office

Ms Ann-Charlotte SMEDLER
National Council on Medical Ethics, Sweden

Ms Marja SORSA
Nordic Committee on Bioethics, Finland

Erling TIEDEMANN
Danish Council of Ethics

Ms Ariane WILLEMSEN
Ethics Committee on Non-Human Gene Technology, Suisse

Representatives of industry

Mr Philippe BOUVET
Aventis Pharma, France

Mr Giampiero DE LUCA
Serono International, Switzerland

Mr Paul HERRLING
Novartis Pharma AG, Switzerland

Mr Joachim KOWALLIK
Akzonobel international, Belgium

Mr Eberhard LAMPETER
VITA 34, Private blood bank, Germany

Mr Enrico LASTREGO
Novartis Management Services sa, Belgium

Ms Catherine LEVINSON,
Serono International, Switzerland

Ms Anne PAPIN-DI POMPEO
European Federation of Pharmaceutical Industries and Associates

Andrea RAPPAGLIOSI
Serono International, Switzerland

Ms Charlotte RETZLER
Serono International, Switzerland

Ms Annie VAN BROEKHOVEN
Innogenetics Nv, Belgium

Representatives of associations

Mr Markku AARIMAA
Comité permanent des Médecins européens (CP)

Mr Georges BINAME
Association belge de bioéthique

Mr Adrian VAN BELLEN
The Netherlands Dutch Genetic Alliance of Parent/Patient Organisations

Mr Ben DUNCAN
British Medical Association

Ms Susanne DÖRING
German Medical Association

Mr Christoph THEN
Greenpeace, Germany

Representatives of religion

MS Heidrun BACK
Büro Brüssel des Bevollmächtigten des Rates der Evangelischen Kirche in Deutschland (EKD)

Mr Silvio MARCUS-HELMONS
Commission of the Bishop's Conferences of the EU

Mr Panagiotis MOSCHONAS
Représentation de l'Eglise de Grèce auprès de l'UE

Ms Katharina SCHAUER
Commission of the Bishop's Conferences of the EU

Academics

Ms Danielle BERNEMAN
Institut Pasteur, Paris, France

Mr Maurice DE WACHTER
Consultant Bioethics, Belgium

Ms Donna DICKENSON
Centre for the Study of Global Ethics
University of Birmingham, United Kingdom

Ms Christine DOSQUET
Unité de thérapie cellulaire et espace éthique
Hôpital Saint-Louis, Paris, France

Ms Anne-Françoise GILLARDIN
Centre de génétique humaine, Belgium

Mr Sefik GÖRKEY
Medical Ethics Department
Marmara University, Faculty of Medecine
Istanbul, Turkey

Mr Bart HANSEN
Centre for Biomedical Ethics and Law
Catholic University Leuven, Belgium

Mr Paul JANIAUD
Institut National de Recherche Médicale
(INSERM), Belgium

Prof. Outi HOVATTA
Huddinge University Hospital, Sweden

Mr Jean-Noël MISSA
Centre de Recherches Interdisciplinaires
en Bioéthiques, Belgium

Mr Jacques SCHERES
Clinical Genetics Centre, Academic Hospital
Maastricht, The Netherlands

Ms Christine VERELLEN-DEMOULIN
Centre de génétique humaine, Belgium

Ms Patricia WALSH
Centre of medical ethics and law
Kings College London, Great Britain

Medias

Mr Jean-Michel BADER
Le Figaro, France

Ms Helen BIRD
Cordis News, Belgium

Thomas A. FRIEDRICH
Welt Science, Germany

Mr Paul KING
Cordis News, Belgium

Mr Christophe LENNERT
Katolische Nachrichten – Agentur (KNA)
Germany
Jean-Yves NAU
Le Monde, France

Mr Olivier JEHIN
Agence Europe

Mr Pascal LE SEGRETAIN
Corsis Sygma, France

Secretariat of the European Group on Ethics

Ms Christiane Bardoux

Tel: 32 (0) 2 295 45 47
Fax: 32 (0) 2 299 45 65
E-mail: christiane.bardoux@cec.eu.int

Ms Joelle Bezzan

Tel: 32 (0) 2 296 19 48
Fax: 32 (0) 2 299 45 65
E-mail: joelle.bezzan@cec.eu.int

Ms Marie Chirol

Tel: 32 (0) 2 296 25 84
Fax: 32 (0) 2 299 45 65
E-mail: marie.chirol@cec.eu.int

Ms Agueda Ollero Montiel

Tel: 32 (0) 2 295 71 35
Fax: 32 (0) 2 299 45 65
E-mail: agueda.ollero-montiel@cec.eu.int

Mail address

European Commission
Group of Policy Advisers
BREY 10/128
B – 1049 – Brussels - Belgium

Office

European Commission
Avenue d'Auderghem 45
B – 1049 – Brussels - Belgium

Web site

http://europa.eu.int/comm/european_group_ethics