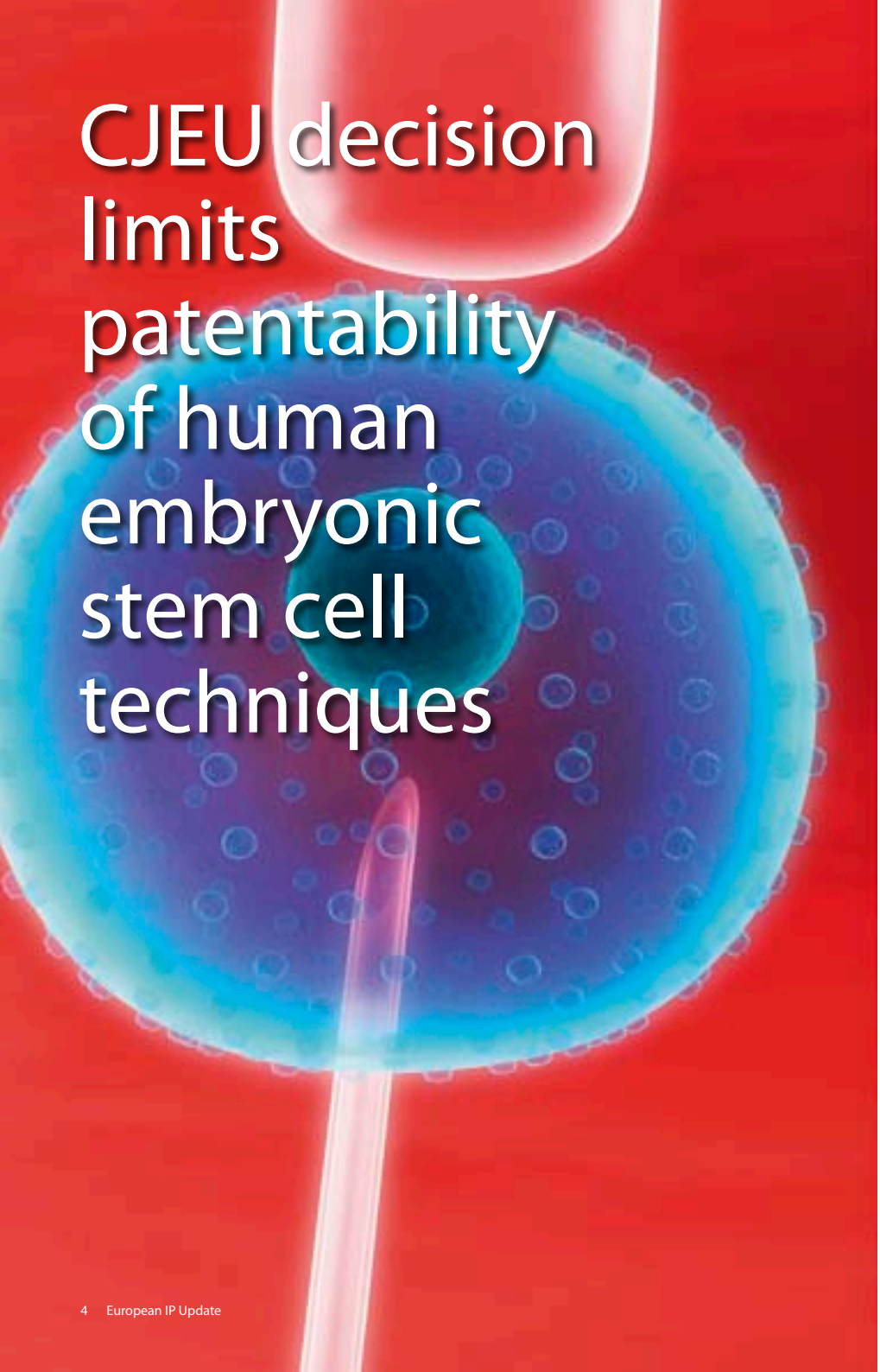
CJEU decision limits patentability of human embryonic stem cell techniques



Technology background

Stem cells are found in almost all multi-cellular organisms. Stem cells are totipotent or pluripotent which means they have the ability to renew themselves and differentiate into a complete organism (=totipotent) or that they have the ability to differentiate into a diverse range of specialized cell types (=pluripotent). There are two types of mammalian stem cells: embryonic stem cells, found in embryos, and adult stem cells, found in various tissues. Embryonic stem cells differentiate into embryonic tissue during the embryo's development. Adult stem cells form a repair system and maintain the turnover of regenerative organs such as blood, skin and intestinal tissue.

Present laws and regulations on research relating to embryonic stem cells

Up until 18 October 2011, there was little direct relevant regulation concerning research relating to embryonic stem cells on the EU level. The Council of Europe's Convention of Human Rights and Biomedicine, which entered into force in 1999, states in Article 18 – that (1) "Where the law allows research on embryos in vitro, it shall ensure adequate protection of the embryo" and (2) "The creation of human embryos for research purposes is prohibited". It is silent on the use of so-called "surplus" embryos. Although the Convention is signed by most member states, however for

Tuesday - 18 October, 2011 - the Court of Justice of the European Union (CJEU) issued a decision on the patentability of embryonic stem cells in the referred case of Brüstle vs. Greenpeace (E-34/10). The court ruled that exclusion from patentability of stem cell techniques using human embryos for industrial or commercial purposes includes research purposes. The court further ruled that any human ovum stimulated by fertilization or parthenogenesis to further development, and carrying the capacity to develop into a complete human, constitutes a human embryo. The court referred back to the national court to decide, in the light of scientific developments, whether a stem cell obtained from a blastocyst is to be considered a human embryo.

instance not by Germany, it is not ratified by member states like the Netherlands, the United Kingdom, France and Italy. No agreement was reached on a draft resolution submitted by the European Parliament in 2003, envisaging support of EU funding for research relating to the use of embryonic stem cells from surplus early stage (i.e. up to 14 days) human embryos created prior to 27 June, 2002.

In the Netherlands, the United Kingdom, France, and Germany research on human embryos is authorized under certain conditions. The specific preconditions set in the national laws for the utilization of stem cells differ between these states, where in this respect Germany can be probably considered as the strictest and the United Kingdom as the most liberal country even authorizing the creation of embryos for research purposes under certain conditions.

Laws, regulations and jurisprudence on patentability of embryonic stem cells

Starting from the late nineties, several laws and regulations concerning the patentability of embryonic stem cells came into force in the European community.

On the EU level, the Directive 98/44/EC on biotechnology inventions, which came into force in 1998 and is binding to the EU community, is concerned specifically with the legal protection of biotechnological inventions. According to Article 6(2)(c) of the Biotech Directive, the use of human embryos for industrial or commercial purposes is not patentable. In addition to this Directive, the European Patent Convention or EPC, the multilateral treaty providing an autonomous grant system for European Patents and which is binding only to the EPC contracting states, prohibits the patentability of inventions for which commercial exploitation would be contrary to "ordre public" or morality (Article 53(c) of the EPC). The latter has literally implemented Article 6(2)(c) of Directive 98/44/EC. As specified in Rule 28(c) of the EPC, the use of human embryos for industrial or commercial purposes is considered as contrary to "ordre public" and therefore not patentable.

In 2004, Wisconsin Alumni Research Foundation (WARF) appealed against the decision of the Examining Division of the European Patent Office or the EPO to refuse the European patent application entitled "Primate embryonic stem cells". The Examining Division had based its decision mainly on the fact that the application as originally filed described the indispensible use of human embryos as starting material for the invention, while the invention did not serve a therapeutic or diagnostic purpose useful to the embryo.

The EPO's Board of Appeal concerned with the appeal case, decided to refer to the Enlarged Board of Appeal questions concerning the patentability of human embryonic stem cells (T1374/04). In response, in 2008 the Enlarged Board of Appeal decided (G2/06) that Rule 28(c) of the EPC (reading: *European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the use of human embryos for industrial or commercial purposes*) applies to all pending applications including those filed before the rule had entered into force. Furthermore, the Enlarged Board of Appeal decided that Rule 28(c) of the EPC forbids the patenting of claims directed to products which, as described in the application, at the filing date could be prepared exclusively by a method which necessarily involved the destruction of the human embryos from which these products are derived, even if the method is not part of the claims and irrespective of the fact that after the filing date the same products could be obtained without having to recur to a method necessarily involving the destruction of human embryos.

The EPO's Enlarged Board of Appeal thus banned stem cells obtained from human embryos from patentability if those embryos would be destroyed during the process. Interestingly, in their reasoning the Enlarged Boards of Appeal explicitly did not interpret the term embryo since

they considered that any restricted meaning of the term "embryo" would undermine the intention of the legislator of the Directive 98/44/EC.

The appellant WARF already pleaded that as the wording of Rule 28(c) of the EPC repeats the wording of Article 6(2)(c) of the Directive 98/44/EC and as this wording is not free of doubt, the Enlarged Board of Appeal should refer to the CJEU as to how to interpret this law of the European Union. The Board, however, responded stating that only courts or tribunals of a member state of the EU can refer to the CJEU and that the Enlarged Board of Appeal cannot do so.

The case Brüstle vs. Greenpeace opened up the possibility to refer to the CJEU with questions concerning the interpretation of "use of human embryos for industrial or commercial purposes."

Referral to the Court of Justice of the European Union

In 2004, the German Patent Court (Bundesgerichtshof) had declared a patent of Mr. Brüstle relating to isolated and purified neural precursor cells and granted in 1999 invalid insofar as it relates to obtaining the precursor cells from human embryos. The trial was initiated by Greenpeace who pleaded that the Brüstle patent should be declared void of application as the object of the patent requires the use of human embryos. The Court based its decision on paragraph 2.2.3 of the national law on patents (Patentgesetz) stating that "patents shall not be awarded for the use of human embryos for industrial or commercial purposes." Paragraph 2.2.3 is a direct national transposition of Article 6(2)(c) of the Biotech Directive which, as already indicated, dictates that "use of human embryos for industrial or commercial use shall be considered not patentable."

Mr. Brüstle appealed against the decision and in 2009 the German Federal Court stayed the proceedings for referring interpretation questions to the CJEU. Namely, Mr. Brüstle had inter alia pleaded that the stem cell lines according to his invention were harvested from blastocysts 4 to 5 days after fertilization, while according to several European countries the term embryo is only used starting from 14 days after fertilization. Hence, the stem cell lines according to his invention would not be harvested from embryos, because a blastocyst is not an embryo yet. In line with the statement of WARF in G2/06, Mr. Brüstle stated that Article 6(2)(c) of Directive 98/44/EC lacks a definition of the term "human embryo".

In the light of the debate, the German Federal Court decided to refer the following questions to the CJEU:

1. What is meant by the term "human embryos" in Article 6(2)(c) of Directive 98/44/EC?
   (a) Does it include all stages of the development of human life, beginning with the fertilization of the ovum, or must further requirements, such as the attainment of a certain stage of development, be satisfied?
   (b) Are the following organisms also included?
   - unfertilized human ova into which a cell nucleus from a mature human cell has been transplanted;
   - unfertilized human ova whose division and further development have been stimulated by parthenogenesis?
   (c) Are stem cells obtained from human embryos at the blastocyst stage also included?
2. What is meant by the expression "uses of human embryos for industrial or commercial purposes? Does it include any commercial exploitation within the meaning of Article 6(1) of the Biotech Directive, more in particular, does it include use for scientific research purposes?
3. Is technical teaching to be considered not patentable pursuant to Article 6(2)(c) of Directive 98/44/EC even if the use of human embryos does not form part of the technical teaching claimed with the patent, but is a necessary precondition for the application of that teaching?
   (a) because the patent concerns a product whose production necessitates the prior destruction of human embryos, or
   (b) because the patent concerns a process for which such a product is needed as base material?

Judgment of the Court of Justice of the European Union

The CJEU answered the questions as follows:

1. Any human ovum after fertilization, any non-fertilized human ovum into which the cell nucleus from a mature human cell has been transplanted, and any non-fertilized human ovum whose division and further development have been stimulated by parthenogenesis constitute a human embryo.
   It is for the referring court to ascertain, in the light of scientific developments, whether a stem cell obtained from a human embryo at the blastocyst stage constitutes a human embryo within the meaning of Article 6(2)(c) of Directive 98/44/EC.
2. The exclusion from patentability concerning the use of human embryos for industrial or commercial purposes also covers the use of human embryos for scientific research purposes. Only use for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it are patentable.
3. An invention is excluded from patentability if

the technical teaching which is the subject matter of the patent application requires the prior destruction of human embryos or their use as base material, whatever the stage involved and even if the description of the technical teaching claimed does not refer to the use of human embryos.

Implications of the Judgment of the Court

Throughout the Judgment, the Court and also the Advocate General in his opinion, stated that the decision and opinion are based on the fact that deriving embryonic stem cells from a blastocyst inevitably leads to the destruction of the blastocyst. According to the Court, the "use for industrial or commercial purposes" has to be interpreted broadly, and only the "use for therapeutic or diagnostic purposes which are applied to the human embryo and are useful" can be considered a patentable exception. The Advocate General in his opinion reasoned that inventions relating to pluripotent stem cells obtained without destroying or modifying an embryo could be patentable. The latter would allow for the patentability of inventions relating to embryonic stem cells obtained from for somatic cells (Takahashi and Yamanaka, Cell 126: 663-76, 2006; Yamanaka et al., Cell 131: 1–12, 2007) or derived from a blastocyst if such a method does not lead to the destruction or even to the modification of the developing embryo, which seems conceivable regarding existing embryo diagnostic techniques (blastocyst biopsy). The Advocate General's opinion is here in line with the EPO's Enlarged Board of Appeal.

The Court, however, does not fully share the Advocate General's opinion, as the latter's statement that inventions relating to pluripotent stem cells obtained without destroying or modifying an embryo can be patentable is not

repeated in the Judgment of the Court. In fact, the Court stated that the possible capability of a cell isolated from a blastocyst to develop into a human embryo is decisive whether or not embryonic stem cells obtained from a blastocyst are patentable (inter alia point 37 of the Judgment). In the light of the first part of answers 1 and 3 given by the Court, this statement and the referral to the national court to decide on the patentability of a stem cell obtained from a blastocyst in answer 1, seems redundant. As it appears from the first part of answer 1 according to which a blastocyst is to be included in the 'human embryo' concept while answer 3 rules that an invention is excluded from patentability where the technical teaching requires the prior use of human embryos as base material, it directly follows that a stem cell obtained from a blastocyst is not patentable.

Answer 3 of the CJEU is in agreement with the earlier decision of the EPO's Enlarged Board of Appeal and takes this further. In its decision in case G 2/06, the Enlarged Board of Appeal reached the same conclusion that whenever the subject matter requires the prior destruction of human embryos or their use as base material, even if this has occurred in a stage long before the actual subject matter of the patent application, the subject matter is excluded from patentability. The CJEU takes this further because it rules that stem cells obtained by a technique that does not destroy the embryo are also banned from patentability.

Concluding remarks

Although leaving an apparent fictitious opening for stem cell inventions derived from blastocysts, the decision will have significant impact on embryonic stem cell research as it bans the patentability on almost any invention relating to embryonic stem cell techniques in Europe.

Other than the EPO, the CJEU also ruled on the question whether artificially created (totipotent) stem cells also fall under the definition of human embryo. The fact that the CJEU rules that such stem cells are also to be regarded as human embryos, and that inventions necessitating the destruction of such cells are not patentable may have significant impact on commercial stem cell research in Europe.

According to the opinion of the Advocate General, insofar it is or will become possible to obtain pluripotent stem cells without destroying an entity that was capable of developing into a human being, inventions like that of Mr. Brüstle could have been patentable after all. However, the Judgment of the Court does not repeat this statement. Accordingly, it is conceivable that stem cell research in Europe will be limited even beyond G2/06. The EPO applied G2/06 in such a way that claims relating to (deposited) embryonic stem cells filed after May 2003 were allowable as from this date on, deposited stem cells could be obtained without having to destroy embryos. According to the present judgment, this may no longer be possible.
It will be quite interesting to see what steps the EPO will take with respect to the present CJEU ruling. In theory the EPO has three options:

1) implement the CJEU judgment, thereby applying the judgment also to non-EU contracting states to the EPC; the non-EU contracting states would keep the possibility to deviate from the CJEU judgment by converting the European patent application into a national application pursuant to Article 135 of the EPC, or,
2) deny the judgment, which would be inconsistent with the earlier implementation of Directive 98/44/EC 2), or,
3) implement the judgment only for contracting states, allowing different sets of claims for EU and non-EU contracting states, which would be inconsistent with the harmonization objective.

It remains to be seen which of these options the EPO will follow; the first option seems to be the most likely option from both a political and procedural point of view.

The present decision clearly indicates that the CJEU aims at seriously limiting the patentability of results obtained from human embryonic stem cell research, thereby inherently limiting such research in Europe.
Inventions related to therapeutic or diagnostic purposes for the human embryo itself are still patentable. However, when the basic research on human embryonic stem cells that precedes such inventions is discouraged by banning the patentability of results obtained, obviously the devise of such inventions for therapeutic or diagnostic purposes will also be hampered.

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