Preliminary Ruling of the Court of Justice of the European Union in *Oliver Brüstle v. Greenpeace e.V.*: Impacts on Patenting of Human Embryonic Stem Cells in Europe

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THE PATENTING OF TECHNOLOGY based on human embryonic stem cells has been a controversial issue ever since the advent of stem cell technology.

The patentability of stem cells is less restrictive in the U.S. than in Europe. Inventions relating to pluripotent,¹ but not totipotent,² human embryonic stem cells are considered patentable in the U.S., regardless of whether the practice of such inventions involves the destruction of a human embryo.

In Europe, the European Patent Office (EPO) has adopted a stricter approach following the Enlarged Board of Appeal (EBA) decision, G2/06,³ relating to the patentability of human embryonic stem cells. Currently, the EPO is of the view that inventions relating to human embryonic stem cells are not deemed immoral if the invention is obtainable without necessitating the destruction of a human embryo. Furthermore, if the invention involves an established human embryonic stem cell line available at the filing date of the patent application, such inventions are deemed patentable, as no human embryo would have been destroyed. In particular, the EPO established the date at which such established cell lines are considered to be publicly available as of at least May 2003.

The U.K. Intellectual Property Office (IPO) initially adopted a different view from the EPO and issued a practice note in April 2003 stating that patents would not be granted for inventions relating to totipotent cells but would be granted for patents relating to pluripotent or multipotent stem cells. Subsequently, in February 2009, the IPO revised its practice in light of the EBA decision G2/06 to exclude from patentability patents on processes for obtaining stem cells from human embryos or stem

cells that can be obtained only via the destruction of human embryos.

BACKGROUND

A German patent was granted to Professor Oliver Brüstle in 1999 relating to isolated and purified neural precursor cells produced from human embryonic stem cells for the treatment of neural disorders, processes for producing them, and uses thereof.

The patent was declared invalid by the German Patent Court following a nullity action filed by Greenpeace. Greenpeace had argued that the patent was contrary to public order and morality, and more specifically prohibited by Article 6(2)(c) of the Biotechnology Directive,⁴ which states that “uses of human embryos for industrial or commercial purposes” are unpatentable.

Following Brüstle’s appeal to the German Federal Court of Justice (Bundespatentgericht), proceedings were stayed, as the court considered it necessary to refer several questions to the Court of Justice of the European Union (CJEU). In particular, the German Federal Court of Justice was of the view that the concept of “human embryo” required further clarification, as it is notably undefined in Article 6(2)(c) of the Biotechnology Directive.

¹Defined in the case as cells produced at the later blastocyst stage of the embryo that can no longer differentiate into all cell types of the body.

²Defined in the case as cells produced at the earliest stages of development after fertilization that can differentiate into all embryonic and adult cell types of the body.

³G2/06: Official Journal EPO 5/2009, 306.

⁴Directive 98/44/EC on the legal protection of biotechnology inventions.

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THE SCOPE OF THE BIOTECHNOLOGY DIRECTIVE

In 1998, the Biotechnology Directive was introduced with the intention of harmonizing the patenting of biotechnology inventions in the EU. The Directive prohibited the grant of patents that were contrary to morality, such as processes for cloning human beings and the use of human embryos for industrial or commercial purposes.

The German Federal Court of Justice referred the following three questions to the CJEU for a preliminary ruling on the scope of Article 6 of the Biotechnology Directive:

1. What is meant by the term “human embryos” in Article 6(2)(c) [of the Directive]?
 - (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 Directive]—especially use for the purposes of scientific research?
3. Is technical teaching to be considered unpatentable pursuant to Article 6(2) (c) of the Directive even if the use of human embryos does not form part of the technical teaching claimed within the patent, but is a necessary precondition for the application of that teaching:
 - because the patent concerns a product whose production necessitates the prior destruction of human embryos,
 - or because the patent concerns a process for which such a product is needed as base material?

In accordance with the procedure before the CJEU, an Advocate General issued an opinion on the case, and subsequently, the judges of the CJEU issued their judgment.

THE ADVOCATE GENERAL’S OPINION

Advocate General (AG) Yves Bot issued his opinion on the referred questions on 10 March 2011.

The basis of the decision derived from the wording of Article 5(1) of the Biotechnology Directive, which aims to protect “the human body, at the various stages of its formation and development.”

Bearing this aim in mind, the AG differentiated between totipotent and pluripotent cells. Specifically, the AG gave his opinion that totipotent cells have the capacity to develop into a complete human being and stated that “thus, those cells, since they represent the first stage of the human body which they will become must be legally classified as embryos, the patentability of which must be excluded.” Therefore, this definition also encompasses unfertilized ova into which a cell nucleus from a mature cell has been transplanted (somatic cell nucleus transfer) and unfertilized ova whose division has been stimulated by parthenogenesis.

Pluripotent embryonic stem cells, however, were considered by the AG not to fall within the definition of an embryo “since individually, they are no longer capable of developing into a human being.” The reasoning for this finding was based on the fact that pluripotent cells can differentiate “only” into various organs forming parts of the human body rather than a complete human being.

The AG considered that although the patent in question related to cells derived from the blastocyst stage (pluripotent cells), it was not possible to ignore the origin of such embryonic stem cells. In view of this, the AG also pointed out that “inventions relating to pluripotent stem cells can be patentable only if they are not obtained to the detriment of an embryo, be that its destruction or its modification.”

In conclusion, the AG was of the opinion that an invention cannot be regarded as patentable where the application of the technical process for which the patent is filed necessitates the prior destruction of human embryos or their use as base material, even if the description of the process does not specifically mention the use of human embryos.

The AG did observe, however, that the patentability of uses of human embryos for industrial or commercial purposes is not prohibited under the Directive where it concerns only inventions for therapeutic or diagnostic purposes that are applied to the human embryo and are useful to it.

PRELIMINARY RULING BY THE CJEU

The AG’s opinion was broadly adopted in the judgment of the CJEU, issued on 18 October 2011.⁵

⁵*Oliver Brüstle v Greenpeace, Case C-34/10.*

Ruling on Question 1: What is meant by the term “human embryos”?

The CJEU first discussed how the definition of “human embryo” is an extremely sensitive social issue in many member states and, bearing this in mind, the court “is not called upon to broach questions of a medical or ethical nature, but must restrict itself to a legal interpretation of the relevant provisions of the Biotech Directive.”

The Court then noted that although the Preamble to the Directive seeks to promote investment in the field of biotechnology, Recital 16 emphasizes that “patent law must be applied so as to respect the fundamental principles safeguarding the dignity and integrity of the person.” In view of this, the court considered that the context and aim of the Directive was that European Union legislature should exclude any possibility of patentability where human dignity could be affected. In turn, the court concluded that the concept of “human embryo” according to Article 6 of the Directive should be understood in a wide sense.

The court thus concluded that any human ovum must, as soon as fertilized, be considered as a “human embryo” within the meaning of Article 6(2)(c) of the Directive, if that fertilization is such as to commence the process of development of a human being.

Furthermore, such a classification also extended to a non-fertilized human ovum into which the cell nucleus from a mature human cell has been transplanted and a non-fertilized human ovum whose division and further development have been stimulated by parthenogenesis. The court reasoned that “although those organisms have not, strictly speaking, been the object of fertilization, due to the effect of the technique used to obtain them they are capable of commencing the process of a development of a human being, just as an embryo created by fertilization of an ovum can do so.”

In relation to stem cells obtained from a human embryo at the blastocyst stage, the court concluded that it is for the referring court to ascertain, in the light of scientific developments, whether they are capable of commencing the process of development of a human being and, therefore, are included within the concept of “human embryo” according to Article 6(2)(c) of the Directive.

Notably, the court differed in its approach from the AG on the point regarding pluripotent cells obtained from the blastocyst stage. The AG had concluded that pluripotent cells fell outside the definition of “human embryo” provided they were obtained without the destruction of a human embryo.

It remains to be seen whether the referring court, in this case, the German Federal Court of Justice does indeed consider the pluripotent cells obtained from the blastocyst to fall within the definition of a “human embryo.”

Ruling on Question 2: What is meant by “uses of human embryos for industrial or commercial purposes”?

In relation to the second question, the court stated that the purpose of the Directive is not to regulate the use of human embryos in the context of scientific research. It is limited to the patentability of biotechnology inventions.

The court concluded that although the aim of scientific research must be distinguished from industrial or commercial purposes, the use of human embryos for the purposes of research that constitutes the subject-matter of a patent application cannot be separated from the patent itself and the rights attaching to it.

In conclusion, the court ruled that “the exclusion from patentability concerning the use of human embryos for industrial or commercial purposes set out in Article 6(2)(c) of Directive 98/44 also covers the use of human embryos for scientific research, only use for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it being patentable.”

Ruling on Question 3: What is the extent of exclusion for the use of human embryos?

The final issue that required clarification concerned whether an invention is unpatentable even though its purpose is not the use of human embryos, where it relates to a product whose production necessitates the prior destruction of human embryos or a process for which requires a base material obtained by destruction of human embryos.

The court raised the point that with respect to the patent-in-suit, although the claims did not specifically mention human embryonic stem cells, the removal of a stem cell from a human embryo at the blastocyst stage entailed destruction of that human embryo as of the date in question. Therefore, “the fact that destruction may occur at a stage long before the implementation of the invention as in the case of the production of embryonic stem cells from a lineage of stem cells the mere production of which implied the destruction of human embryos is, in that regard, irrelevant.”

In conclusion, the court ruled that “Article 6(2)(c) of Directive 98/44/EC excludes an invention from patentability where 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* at which that takes place and even if the description of the technical teaching claimed does not refer to the use of human embryos.”

The CJEU were of the view that to not include subject matter in the scope of the exclusion on the grounds that such subject-matter does not refer to the use of

human embryos would make the provision redundant by allowing a patent applicant to avoid its application by skillful drafting.

AN UNCERTAIN FUTURE IN EUROPE

Essentially, the CJEU decision has confirmed and clarified the comments made by the AG.

It is important to consider how this decision will interplay with the G2/06 EBA decision issued on 25 November 2008. In G2/06, it was held that a patent cannot be granted for an invention which *necessarily involves* the use and destruction of a human embryo.

Following G2/06, the EPO have adopted the current policy whereby patents directed to products derived from human embryonic stem cell lines where their filing date is after May 2003 are not necessarily excluded from patentability. The reasoning is based on the fact that such human embryonic stem cell lines have been made publicly available on their deposit at specific institutions such as the U.S. National Institute of Health, meaning that no detriment to the human em-

bryo is caused in order to practice the claimed invention.

Although the CJEU decision is not formally binding on the EPO, it will be interesting to see whether the EPO will continue with its current practice or whether it is likely to reassess in view of the phrase “*whatever the stage at which* [the destruction of a human embryo] *takes place*” cited by the CJEU. The case for discussion could arise where it was necessary to destroy a human embryo in order to generate the deposited stem cell line and so, following the reasoning of the CJEU, a product derived from such a stem cell line should be excluded from patentability.

From a commercial perspective, the CJEU ruling should not affect companies from securing patent protection in the U.S. or Asia. However, there are fears that investment in the stem cell field in the EU may be affected in light of the CJEU decision which is binding on the courts of the EU member states.

[*BLR* published another story on this subject at 31 Biotech. L. Rep. 49. Excerpts from the decision can be found at 31 Biotech. L. Rep. 60.]

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