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Brüstle v. Greenpeace: implications for stem cell research

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On 10 March 2011, the Advocate General of the Court of Justice for the European Union issued an Opinion, which essentially recommended that certain inventions related to human embryonic stem cells should not be patentable. Since the publication of the Opinion, the case (*Brüstle v. Greenpeace* Case C-34/10) has generated a lot of commentary, including numerous articles and discussion in the UK parliament. This article will seek to summarize the case and discuss its practical ramifications.

Background

In 1997, Professor Oliver Brüstle filed an application in Germany for a patent entitled 'Neural Precursor Cells, Method For The Production And Use Thereof In Neural Defect Therapy'. The patent related to methods of converting human embryonic stem cells (hESCs) into neural precursor cells that may treat neurological trauma and disease (such as Parkinson's disease and multiple sclerosis).

Greenpeace sought to annul the patent pursuant to Article 6(2)(c) of the European Biotech Directive [1] on the basis that the cells came from an embryo, which had to be destroyed in order to harvest the cells.

The issue arises as a result of a provision in the Biotech Directive 1998, which prohibits patents related to the commodification of embryos. Article 6(2)(c) of the Biotech Directive excludes from patentability "uses of human embryos for industrial or commercial purposes" on the basis that such patents would be "contrary to order public or morality".

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Questions referred to the court

The Court of Justice for the European Union (CJEU) was asked to consider a number of questions. However, we will focus on the two that attracted most discussion:

n Does the prohibition extend to a blastocyst, which has lost its ability to become a human being?

n Is a matter unpatentable 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?

Opinion of the Advocate General

As regards specific types of cells, the Advocate General stated as follows:

"Totipotent cells carry within each of them the capacity to develop into a complete human being: they represent the first stage of the human body which they will become and must be classified as embryos."

(Totipotent cells created through cell nuclear transfer or parthenogenesis would also be embryos for these purposes); and:

"While pluripotent hESCs obtained from a blastocyst do not fall within the

definition of an embryo (as they are no longer capable of developing into a complete human being), it is not possible to ignore the origin of these cells, and a patent should be excluded if the technical process necessitates the prior destruction of an embryo."

Similarly, the Advocate General briefly dismissed the question of whether the patent needs to expressly refer to the destruction of the embryo. While his language was colourful (including drawing a bizarre comparison with organ trafficking from concentration camps in the former Yugoslavia), the crucial paragraph (117) regarding patentability provides:

"An invention must be excluded from patentability 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 that process does not contain any reference to the use of human embryos."

What patents would actually be prohibited?

This language is slightly different to the position currently adopted by the European Patent Office since the Wisconsin Alumni Research Foundation

decision in November 2008, which prohibits “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” human embryos.

While the Advocate General’s Opinion is not clear, it may go further than the current position.

- **First**, the current regime only rejects patents for products produced exclusively by a method that destroyed an embryo. This left open the so-called ‘deposit loophole’ if the patentee deposits a sample at a recognised depository prior to the patent filing date. Depositing the sample avoids the conclusion that the product exclusively necessitated destruction of an embryo.
- **Second**, the current regime only refers to matters described in the application itself, while the Advocate General suggests that it would be appropriate to look behind the patent application. While this could expand the prohibition, it is also possible that, by looking behind the patent application itself, the prohibition is actually narrowed. By way of example, it is possible that a patent may be granted if the patentee can point to technical means in existence at the time of the patent application by which a hESC line could be created without the need to destroy the embryo. This may save the patent even if that procedure was not used in relation to the patented product.

Inconsistent with national laws in member states

Without seeking to comment on the ethics of the use of supernumerary *in vitro* fertilization embryos, it is worth noting that this Opinion appears inconsistent with the national laws in various European States. For example, in the UK, the creation and use of hESC lines is considered mor-

ally acceptable. Each aspect of the creation, development and use of hESCs in the UK is permitted. As a result, there are numerous research projects in the UK today involving hESCs and cell lines. In fact, the UK Stem Cell Bank was established to promote stem cell research in the UK. In order to minimize the number of embryos used, every embryonic stem cell line derived in the UK must be deposited in the UK Stem Cell Bank, which other researchers can access.

Inconsistent with international position regarding patentability of hESC inventions

This Opinion is at odds with the approach in most other countries, including the USA, where there is no legal objection to the grant of such patents. Thus, if the Court adopts the Opinion, then an invention regarding hESCs that would be patentable in the USA would not be patentable in the EU. This is the case irrespective of where the research is conducted; so researchers outside Europe will be as affected as researchers within Europe.

Ramifications if the CJEU adopts the Opinion

Prior to discussing the ramifications of any decision, it is worth emphasizing that this is merely a precursor to the decision of the Grand Chamber of the court of the CJEU, which is expected later in 2011. While the court tends to adopt the Opinion of its Advocate General, this is not mandatory. However, the decision of the CJEU will not be appealable and must be followed by the national courts in each Member State in the EU.

n No impact on the legality of hESC research or therapies in Europe

The first point to make is that, if the Court adopts the Opinion, this will not have any effect on the existing patchwork of legislation regarding

the conduct of hESC research in the Member States of the EU. The decision will be limited to the availability of patents regarding certain types of inventions involving hESCs.

n Other forms of protection

It is worth noting that, even if the Court adopts the Opinion, many therapies in the field will be able to take advantage of other forms of protection (so-called ‘Regulatory IP’) that may be at least as valuable as patent protection in certain circumstances.

Orphan drug designation: If a product qualifies for orphan drug designation (if it is intended for the diagnosis, prevention or treatment of a life-threatening or debilitating condition affecting not more than five in 10,000 persons), then, for 10 years after designation, no European regulator may accept another application for a marketing authorization for the same therapeutic indication in respect of a similar medicinal product. Many hESC products will qualify as orphan drugs.

Clinical data exclusivity: Once a new medicine is approved, no generic version of that medicine can be approved using the clinical data that supported the original medicine for a period of 8 years. Thus, anyone seeking to create a generic (or biosimilar) version of a hESC-based medicine would need to conduct their own clinical trials or wait for this 8-year period to expire before they seek to obtain a marketing authorization. During a further 2-year period, no such biosimilar medicine may be marketed anywhere in Europe.

This raises a broader question as to whether any competent authority will accept that there could be a biosimilar version of a hESC-based medicinal product. Given the difficulty that biosimilar monoclonal antibodies have faced to date, the

prospect of a vastly more complex product (namely a stem cell) being considered biocompatible seems implausible in the near future.

n Patents available in many other countries

As mentioned previously, inventions related to hESC lines are patentable in many other countries, including the USA. As a result, even if there is no patent protection available in Europe, the inventor should be able to obtain patent protection (should they want

it) in non-European markets.

In summary, while the Opinion issued by the Advocate General on 10 March 2011 was negative for the sector, the practical consequences of a rejection of Professor Brüstle's patent may be much more limited than some commentators have suggested.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with

a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Bibliography

- 1 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions.