New guidance on the patentability of embryonic stem cell patents in Europe

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The European Patent Office rules in the latest installment of the prosecution of the WARF patents.

At the end of last year, the highest appeal board of the European Patent Office (EPO), the Enlarged Board of Appeal (EBA), issued its eagerly awaited decision regarding the patentability of embryonic stem cells[1]. The proceedings concerned an application filed by the Wisconsin Alumni Research Foundation (WARF) based on the research carried out by James Thomson of the University of Wisconsin in the late 1990s on the derivation of human embryonic stem (hES) cell lines. The WARF patents arising from Thomson's research have proven to be hugely controversial for ethical and commercial reasons and have been subject to proceedings before the US Patent and Trademark Office (USPTO) and the EPO. The ruling from the EBA sets out the EPO's policy on the patentability of hES cells and, at a higher level, the nature of the relationship between the EPO and the European Union (EU) on the issue of biotech patents.

WARF in Europe

The European WARF patent application[2] entitled "Primate embryonic stem cells" was filed in 1996 and was initially rejected by the examining division of the EPO in 2004. This was in part because the method disclosed in the application for obtaining stem cells used, as the starting material, a primate (including human) embryo, which was destroyed in the process. This was found to be in breach of the provisions of the European Patent Convention (EPC), which were introduced as a result of the adoption of the EU's Biotechnology Directive[3] in 1998. Article 5 of the Biotechnology Directive states that the simple discovery of one element of the human body cannot constitute a patentable invention unless it is isolated by means of a technical process. Article 6 states that inventions are considered unpatentable where their commercial exploitation would be contrary to "*ordre public*" or morality, and specifically states that the use of human embryos for industrial or commercial purposes shall be considered unpatentable[4].

WARF appealed this decision to the Technical Board of Appeal and in late 2005 the Board referred four questions to the EBA, the supreme judicial body of the EPO which is responsible for ensuring the uniform application of the EPC. WARF also requested that the EBA should refer the issue of the interpretation of the Biotechnology Directive to the European Court of Justice as it involved the application of EU law.

The EPO versus the EU

The Biotechnology Directive was adopted in 1998 after a protracted series of negotiations between the member states of the EU. Some member states were in favor of patents covering biotech inventions, whereas others were considerably less keen. This tension in Europe still exists some ten years later as evidenced by the fact that the Directive was not implemented into national law by all member states until 2007. However, the Directive was rapidly adopted by the EPO in 1999. The EPC has always included a series of exceptions to patentability, one of which was where the publication or exploitation of an invention would be contrary to *ordre public* or morality[4]. The implementation of the Biotechnology Directive resulted in new guidance on interpreting the morality exception with respect to biotech inventions in the form of Rule 28(c) of the Implementing Regulations to the EPC. The rule states that patents should not be granted to biotechnological inventions that use human embryos for industrial or commercial purposes. However, a recital[5] to the Biotechnology Directive states that this exclusion does not apply for inventions for therapeutic or diagnostic purposes that are applied to the human embryo and are useful to it. In view of the relevance of the Biotechnology Directive to the interpretation of the provisions of the EPC in issue, WARF requested that the referred points be further referred to the European Court of Justice. The EBA refused WARF's request to make a reference to the Court as there was a lack of any legal and institutional link between the EPO and the EU and there was no mechanism for making a reference to the Court. Having rejected WARF's request, the EBA proceeded to consider the four questions referred by the Technical Board of Appeal.

The EBA's ruling

The four questions considered by the EBA, which were initially raised in a similar form by WARF but which were amended and finalized by the Technical Board of Appeal, were as follows:

1. Did the prohibition in respect of biotechnological inventions concerning the use of human embryos for industrial or commercial purposes apply retrospectively to applications filed before the implementation of the Biotechnology Directive into the EPC?

2. If the answer to question 1 was yes, did it make any difference to the validity of the application that the method involving the destruction of human embryos did not form part of the claims?

3. If the answer to question 1 or question 2 was no, did the prohibition under the EPC to inventions contrary to morality apply?

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4. In the context of question 2 and question 3, did it make any difference that after the filing date the products claimed could have been obtained without using the method which involved the destruction of human embryos?

On assessing question 1 the EBA noted that no transitional provisions were made when the Biotechnology Directive was implemented by the EPO and there was no indication that the commercial exploitation of embryos had previously been regarded as patentable. Therefore, the prohibition concerning the use of human embryos for industrial or commercial purposes applied to all pending applications retrospectively. For question 2, the EBA noted that the aim of the implementing rules was to align the EPC with the Biotechnology Directive and that the Directive was to be used as a supplementary means of interpretation. The EBA noted that the prohibition was not limited to claims to the use of human embryos so it was necessary to consider the teaching of the application as a whole rather than just the explicit text of the claims. As the invention described in the WARF application could be performed only by destroying human embryos and the invention was of commercial and/or industrial benefit, it clearly fell within the scope of the prohibition on using human embryos for industrial or commercial purposes. Furthermore, the EBA observed that the exception for inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it did not apply, as the invention had to benefit the embryo itself, and this was not the case in the present application as the embryos used to perform the invention were destroyed.

Given that the answers to questions 1 and 2 were yes, the EBA decided it was not necessary to answer question 3. However, in dealing with question 2, the EBA did note that it was not patenting itself that was considered to be against *ordre public* or morality but the performing of the invention (which in the present case involved the destruction of a human embryo) that had to be considered to contravene these concepts. With respect to question 4, the EBA ruled that technical developments which became publicly available only after the filing date could not be taken into consideration. Therefore, it was irrelevant that after the filing date the same products could have been obtained without having to use the method which necessarily involved the destruction of human embryos. The EBA did not specifically consider the advent of induced pluripotent stem cell lines when dealing with question 4.

The impact of the EBA's ruling

The ruling of the EBA makes it clear for once and for all that any applications for stem cell patents that involve the destruction of human embryos will be not granted. The decision will also remove the blockade on the prosecution of numerous applications at the EPO that were stayed pending the outcome of the WARF case. The ruling means that if the invention of any pending application requires the destruction of embryos, regardless of the product or method claimed, the application will be refused by the EPO.

Nonetheless, patent protection for methods and for human stem cells *per se* based upon cells derived from existing cell lines would appear to be unaffected by the ruling. Indeed, the EBA was keen not to cast doubt on the patentability of human stem cells in general and made it clear at the end of their decision that the ruling was not concerned with the patentability in general of inventions relating to human stem cells or human stem cell cultures. Given the recent advances in stem cell technology, such as the induction of pluripotent stem cells, which do not involve embryo destruction, this indication from the EBA will be warmly welcomed by researchers in the field wishing to file applications. Indeed, Geron, the exclusive licensee of the WARF patents, commented that the decision should not adversely effect its patent applications relating to research performed using existing hES cell lines available from stem cell banks. Furthermore, Geron has since announced that it has received clearance from the US Food and Drug Administration to begin the world's first human clinical trial of hES cell-based therapy for patients with acute spinal cord injury.

In view of the importance of the ruling, the practice of national patent offices is likely to be altered to follow the EPO's policy. The UK Intellectual Property (IP) Office has already issued a new practice notice[6] as a result of the EBA's ruling, which supersedes the UK IP Office's previous practice notice regarding inventions involving hES cells and marks a significant change in policy. The new practice notice makes it clear that the UK IP Office will not grant patents for processes of obtaining stem cells from human embryos and that it will not grant patents for human totipotent cells which have the potential to develop into an entire human body. However, the UK IP Office has decided that the commercial exploitation of inventions concerning human embryonic pluripotent stem cells would not be contrary to public policy or morality in the UK. Therefore, the UK IP Office will continue to grant patents for inventions involving such cells provided they satisfy the normal requirements for patentability and, in accordance with the EBA's ruling, provided that at the filing or priority date, the invention could be obtained by means other than the destruction of human embryos. It will be interesting to see if national patent offices elsewhere in Europe follow the approach adopted in the UK.

The ruling is also notable for distinguishing the EPO from the EU. The EPO sees itself as an international organization not all of whose members are EU member states and, in its view, the EPC contracting states cannot be presumed to have conferred jurisdiction to the European Court of Justice. However, it is conceivable that the questions raised in the present case could arise before the European Court of Justice if the court of a member state applied the Directive and made a reference to the European Court of Justice regarding the meaning of the Directive. Given the divergent approaches taken towards the patenting of stem cells in Europe from relatively permissive regimes, for instance in the UK, to more restrictive regimes such as in Germany, the likelihood of such a reference in the future is not inconceivable. Indeed there is currently a reference pending before the European Court of Justice concerning other aspects of the interpretation of the Biotechnology Directive arising from proceedings in Holland[7]. The willingness of the EBA not to cast doubt on the patentability of human stem cells in general and to avoid coming under the jurisdiction of the European Court of Justice suggests that the EPO is keen to remain the favored forum for applicants wishing to prosecute stem cell patents rather than filing at each individual, national patent office in Europe. Certainly recent history suggests that the EPO wishes to avoid becoming involved in questions of morality which arise in proceedings in some member states as it views itself solely as the arbiter of the EPC rather than the guardian of Europe's morals concerning biotech inventions.

1. Wisconsin Alumni Research Foundation, G 0002/06, 25 November, 2008.
2. EP 0 770 125.
3. European Directive 98/44/EC on the Legal Protection of Biotechnology Inventions.
4. Article 53(a) of the EPC.
5. Recital 42 of the European Directive 98/44/EC on the Legal Protection of Biotechnology Inventions.
6. UKIPO Practice Notice: Inventions Involving Human Embryonic Stem Cells, 3 February 2009.
7. *Monsanto v. Cefetra*, District Court of The Hague, 249983/HA ZA 05/2885, 19 March 2008.