THE IMMORAL GENE: DOES IT REALLY EXIST?

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Over the last years several European patents were opposed for protecting technology violating the morality requirement under Article 53a EPC. Attempts have been made by the Appeal Boards of the EPO, as well as by amendments introduced into the Implementing Regulations of the EPC, to address this sensitive patentability requirement more precisely. The most recent hot topic coming up in this context is the patentability of stem cells. It is to be expected that this discussion will still go on in the field of biotechnological inventions for the next several years.

Legal Basis

The main criteria of patentability under the European Patent Convention (EPC) are set forth in Article 52 EPC:

Article 52 EPC Patentable inventions
(1) European patents shall be granted for any inventions which are susceptible of industrial application, which are new and which involve an inventive step.
(…)

Article 52 EPC is complemented by a number of Rules laid down in the Implementing Regulations of the EPC. With respect to the patentability of biotechnological inventions, Rule 23(c) EPC is particularly relevant.

Rule 23(c) EPC
Biotechnological inventions shall also be patentable if they concern:
(a) biological material which is isolated from its natural environment or produced by means of a technical process even if it previously occurred in nature
(…)

Rule 23(e) EPC further precises for parts of the human body:

(…)
(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.

To answer the question of what is patentable under the EPC several exemptions in the law further have to be considered, such as Article 53 EPC. It reads:

Article 53 EPC Exceptions to Patentability
European Patents shall not be granted in respect of:
(a) inventions the publication or exploitation of which would be contrary to "ordre public" or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;
(…)

Article 53(a) EPC is consistent with Article 6(1) of the EU Biotechnology Directive. In the first clause of both articles, a violation of “ordre public” or “morality” is stated as a criterion which may bar the patenting of an invention. In

decision T356/93 concerning the patentability of plants and plant genes, one of the Boards of Appeal of the European Patent Office (EPO) attempted to define the terms “public order” and “morality” and arrived at the following results.

Ordre Public:
It is generally accepted that the concept of "ordre public" covers the protection of public security and the physical integrity of individuals as part of society. This concept encompasses also the protection of the environment. Accordingly, under Article 53(a) EPC, inventions the exploitation of which is likely to breach public peace or social order (e.g. through acts of terrorism) or to seriously prejudice the environment are to be excluded from patentability as being contrary to the "ordre public".
(section 5 of the reasons)

Morality:
The concept of morality is related to the belief that some behaviour is right and acceptable, whereas other behaviour is wrong, this belief being founded on the totality of the accepted norms which are deeply rooted in a particular culture. For the purpose of the EPC, the culture in question is the culture inherent in European society and civilisation.
(section 6 of the reasons)

Even if these definitions were generally acknowledged, they leave much room for discussion. For instance, reference is made in this connection to the "European culture" mentioned in the definition of morality. Considering the example that euthanasia legislation and embryo protection is handled differently in the various contracting states of the EPC, it can easily be concluded that diverging concepts of the term “morality” also exist within the European culture. It is therefore indeed very questionable whether any authority, including the EPO, will ultimately be able to develop Europe wide accepted, concrete definitions as a suitable means to examine the relevance of Article 53(a) EPC for the patentability of a given technology.

Article 53 EPC is complemented by Rule 23(d) EPC which refers to specific exceptions of patentability falling within the general concept of morality. Said examples shall assist to give better guidance for what type of invention might be in conflict with the morality requirement.

Rule 23(d) EPC Exceptions to patentability
Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following:
(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.

Rule 23(d) EPC thus provides concrete examples of biotechnological inventions falling under the morality concept of Article 53 EPC. However, once again, the weakness of Rule 23(d) EPC is the absence of any definitions. A definition of the term "embryo" above all is critical in this connection. Since in some legal systems, any totipotent cell taken from an embryo which, if the necessary further prerequisites exist, is capable of dividing and developing into an individual is already regarded as an embryo, the exception of letter (a) could already apply to processes for proliferation of embryonic

stem cells, provided that these are in fact totipotent. A further ambiguity concerns the term “cloning”: it is questionable whether this term means a process for the development of a complete organism whose genomic make-up is identical to that of another organism, or whether simple cell division of an embryonic stem cell, provided this is totipotent and therefore to be regarded as a living being, with the aim of propagation of undifferentiated cells, would also be regarded as “cloning”. Rule 23(d), letter (a) EPC can therefore be interpreted to mean that only processes for propagation of undifferentiated human embryonic stem cells are already regarded as falling under the ban on patenting, or that only processes aimed at producing complete organisms having a genetic make-up which corresponds to that of another organism are unpatentable. From a technical standpoint this requests a wide spectrum of processes potentially affected by this exclusion provision.

In summary, it can be said that the EPC, interpreted strictly on the basis of Rule 23, would preclude only the patentability of human embryonic stem cells, and then only if these human embryonic stem cells were in fact totipotent. On the other hand, all human embryonic stem cells which are not totipotent, i.e. all human embryonic stem cells which lack the potential to develop into a complete organism, should be patentable if they meet the other prerequisites of patenting. In a strict sense, processes for culturing and proliferation of human embryonic stem cells, i.e. their propagation in the undifferentiated state, could only be non-patentable if these stem cells would be totipotent. The patentability of processes for obtaining (isolating, concentrating, selecting) human embryonic stem cells depends in turn on the definition of an embryo. For example, blastocysts four to five days old and used as a source for obtaining stem cells are called embryos in Germany, whereas they are regarded as a pre-embryos in England. Therefore, any process which makes use of taking stem cells from blastocysts might be regarded to be in conflict with Rule 23(d)(c) EPC which excludes uses of human embryos for industrial or commercial purposes from patent protection.

Established EPO Practice

The morality requirement of Article 53(a) EPC played a role in a number of cases before the EPO. In the following, the most relevant cases reflecting the current patent practice of the EPO will be discussed.

The "Onco-mouse" - Patent

In 1985, the European patent application no. 8 530 4490.7 (published as EP 0169672), also known as the “Harvard onco-mouse” patent, was filed with the EPO. The application was refused by the Examining Division in its decision of July 14, 1989 (OJ EPO 1989, 451). The application as refused had a total number of 19 claims, claims 1 and 17 reading as follows:

1. A method for producing a transgenic eucaryotic animal having an increased probability of developing neoplasm, said method comprising introducing into an animal embryo an activated oncogenic sequence.

17. A transgenic non-human eucaryotic animal whose germ cells and somatic cells contain an activated oncogene sequence introduced into said animal, or an ancestor of said animal, at an embryonic stage, said oncogene optionally being further defined according to any one of Claims 3

to 10, said animal preferably being a rodent.

The grounds given for refusal were that the application did not meet the requirements of Articles 53(b) and 83 EPC. The relevance of Article 53(a) EPC was also discussed and a number of questions raised.

The applicants appealed against the decision to refuse their application. In the Appeal proceedings subsequently held, the Board of Appeal stated: The decision as to whether or not Article 53(a) EPC is a bar to patenting the present invention would seem to depend mainly on a careful weighing up of the suffering of animals and possible risks to the environment on the one hand, and the invention's usefulness to mankind on the other. It is the task of the department of first instance to consider these matters in the context of its resumed examination of the case (decision T19/90, OJ EPO 1990, 476, section 5 of the reasons).

The case was remitted to the Examining Division for further prosecution, and finally a patent was granted. Section 4(v) of the reasons for the decision of granting reads: In the overall balance the Examining Division concludes that the present invention cannot be considered immoral or contrary to public order. The provision of a type of test animal useful in cancer research and giving rise to a reduction in the amount of testing on animals together with a low risk connected with the handling of the animals by qualified staff can generally be regarded as beneficial to mankind. A patent should therefore not be denied for the present invention on the grounds of Article 53(a) EPC (V6/92, OJ EPO 1992, 589).

The granted patent was opposed by seventeen opponents. During Opposition proceedings, the patent was amended by introducing an auxiliary request directed to rodents instead of non-human mammalian animals. The decision of the Opposition Division to maintain the patent in amended form was appealed. The Appeal proceedings may be expected to be held in the near future.

The "Relaxin"- Patent

Patent EP 0112149 B1 (the so called “Relaxin”- patent) was granted in April 1991. Claim 1 of the patent reads:

1. A DNA fragment encoding human H2-preprorelaxin, said H2-preprorelaxin having the amino acid sequence as set out in Figure 2.

The patent was subsequently opposed by two opponents. The opponents stated that claim 1 should not be patentable under Article 53(a) EPC for the following reasons:

- in order to repeat the invention, tissue is to be taken from a pregnant woman
- in order to repeat the invention woman have to be dismembered and they are piecemealwise sold to commercial enterprises and, therefore, patenting the claimed sequences would amount to a modern form of slavery
- the patenting of human genes means human life is patented which is intrinsically immoral

The patentee submitted that the woman who donated the tissue used as the starting material for cloning consented to do so within the framework of necessary gynaecological operations and that there is no reason to perceive this as immoral.

The Opposition Division maintained the patent. Headnote III of the decision reads:

The isolation of mRNA encoding a human protein from human tissue is not immoral, nor is the patenting of a DNA fragment encoding human proteins intrinsically unethical (point 6 of the reasons, OJ EPO 1995, 388).

The "Edinburgh"- Patent

Patent EP 695351 B1 (also known as the "Edinburgh"- patent) was granted in December 1999. Claims 47 and 48 of the patent as granted read:

47. A method for preparing a transgenic animal comprising obtaining a desired stem cell according to the method of any of claims 1-36, excising the selectable marker from the desired stem cells and generating the transgenic animal therefrom.

48. A method of preparing a transgenic animal, said animal comprising a selectable marker capable of differential expression in (a) desired stem cells and (b) cells other than desired stem cells, the method comprising; providing a blastocyst; providing animal cells according to any of claims 37-38; introducing the animal cells into the blastocyst; transferring the blastocyst to a recipient; and allowing an embryo to develop to a chimaeric animal to enable germline transmission of the selectable marker.

Since in English the term "animal" includes the species man and in the description of the patent expressly stated that the term "animal cells" is also to include "human cells", it was argued that claims 47 and 48 would have included a method of producing a transgenic (claim 47) or chimeric (claim 48) human. The patent was granted shortly after the EPO implemented the principles of the Biotechnology Directive in the EPC. The patent holder, alarmed by four promptly filed oppositions and the reaction of the public, filed new claims within the opposition period, by which, through insertion of the term "non human" before "animal" into claims 47 and 48, the preparation of transgenic humans should have been excluded from patent protection.

In total, fourteen oppositions were lodged against the patent. In July 2002 oral proceedings took place, during which the patent was maintained in limited scope. The Opposition Division asked whether Rule 23(d), letter (c) EPC, by which the use of embryos for industrial or commercial purposes is excluded from patent protection, in fact excludes from patent protection only embryos or also embryonic stem cells obtained from the embryo. After taking various considerations and articles of the EU Biotechnology Directive into account, the Opposition Division concluded that letter (c) of Rule 23(d) is to be interpreted broadly, i.e. not only the use of embryos expressly referred to in the Rules, but also the stem cells resulting from the use of embryos are regarded as non-patentable.

The Opposition Division then gave intensive consideration to the opinion of the European Group on Ethics in Science and New Technologies of the Commission (EGE), according to which modified embryonic stem cells such as are claimed in the Edinburgh patent, should have been regarded as patentable. The Opposition Division, however, evaluated the conclusions of the EGE as inconsistent, out of line with general patent law principles, and finally illogical, and declined to take it into consideration for finding its judgement.

The main request of the patent holder, which differed from the granted patent only in respect of claims 47 and 48 by the insertion of the term "non human" as

already mentioned, was not allowed. Maintenance of the patent in the amended form was only agreed to after human embryonic stem cells were explicitly excluded both in the process claims and in the product claims. Claims 47 and 48 were omitted in total.

The "Euthanasia Composition" - Patent

Patent EP 0516811 B1 (claiming an "euthanasia composition") was granted in April 1996. Claim 1 of the patent as granted reads:

1. A composition which comprises an aqueous solution comprising,
a. a cardiotoxic compound selected from the group consisting of a quinacrine salt and a chloroquine salt in a cardiotoxic amount; and
b. embutramide in a lethally anesthetic amount.

The respective passage in the description as originally filed reads:

The present invention relates to compositions for providing euthanasia in a mammal which are intended for introduction into the heart of the mammal (…), whereby euthanasia occurs in the mammal.

The patent was opposed by three opponents. The opponents stated that claim 1 should not be patentable under Article 53(a) EPC for the following reasons:

- claims encompass the use of the composition for killing humans
- even if euthanasia among human beings was legal or tolerated in one of the contracting states of the EPC, it was nevertheless contrary to morality
- it is contrary to morality to delay the death of animals with technical means
- the composition could be misused for suicide or criminal activity

The Opposition Division maintained the patent in amended form. In the reasons, the Opposition Division stated:

- (…) the compositions could be used for producing death in all kinds of mammals including human beings (section 2.11)
- the approval or disapproval of the exploitation by national law(s) or regulation(s) does not constitute per se, a sufficient criteria for the purposes of examination under Article 53(a) EPC (section 2.17
- it seems from the discussions going on in public and the recommendation referred to above, that the great majority of the public in Europe does support the strict prohibition against intentional ending of life on request

Therefore, the Opposition Division drew the conclusion that "the subject matter at issue is also contrary to morality within the meaning of Article 53(a) EPC" (section 2.21). And further: "Claims 1-13 which refer in light of the description to all kinds of mammals including human beings, are excluded from patentability under Article 53(a) EPC, since they comprise subject matter the exploitation of which is contrary to "ordre public" and morality within the meaning of that provision." (section 2.24)

Consequently, the patentee had to amend the patent. In its amended form, the passage in the description referred to above reads:

The present invention relates to compositions for providing euthanasia in a

lower *mammal which are intended for introduction into the heart of the* lower *mammal (…), whereby euthanasia occurs in the* lower *mammal.*

Summary and Conclusion

As is apparent from the few proceedings before the EPO that dealt with the exclusion provision of Article 53(a) EPC, in particular the morality aspect therein, it is a difficult task for the Patent Office to fairly apply the sensitive aspect of morality to the examination of a certain technology. One reason for this may be the fact that the EPC requires the Examination Divisions to be composed of technical members who normally do not have a special education in ethics. When it comes to the question of whether a claimed invention may be barred from patenting by the morality requirement of Article 53(a) EPC, the claimed product as such usually does not constitute the problem. What might constitute a problem is the intended use of the claimed product as suggested by the patent application. It appears to be fairly clear that claiming nucleic acids and proteins, cells, micro-organisms, tissue, transgenic plants or transgenic animals as such, is not per se excluded from patent protection under Article 53(a) EPC. An exception from this general rule may be the patentability of human embryonic stem cells, the patentability of which is still under debate. Care should be taken when drafting the patent application so that the intended use of the claimed invention is not in conflict with the morality requirement of Article 53(a) EPC.

It is reasonable to assume that the morality debate in the context of inventions in the field of biotechnology will continue for a while, since new technologies frequently surface in this highly progressive field. The next debate on the horizon is already visible in the form of European Patent 112015, which relates to a method of vitrification of a biological specimen, and for which Greenpeace has already announced its intention to file an opposition against.

The debate will go on…