The Patentability and Protection of Living Organisms in the European Union

DR DENIS SCHERTENLEIB
Dr Denis Schertenleib, Solicitor in England and Wales, Registered at the Paris Bar, PhD in Molecular Biology, Associate at Cabinet Hirsch, Paris

As biotechnology has developed in the last 20 years, the subject-matter of the patents generated has evolved from protein sequences or DNA fragments to patents on living organisms including viruses, bacteria, plants and animals. Apart from the ethical and political problems involved with such a subject-matter, more technical problems have arisen in relation to the interpretation and scope of such patent claims. As the value of a patent is in the protection that it confers, these issues are the fundamental ones in this field.

Until recently, the case law of the European Patent Office (EPO) has resulted in the unpatentability of biotechnological inventions involving transgenic plants.

Rather than becoming clearer, the issues have become more complex. Aware of that fact, the European Union issued a directive on biotechnology to ensure uniformity. While this is welcome progress, it has generated questions of its own.

In this article, the legal basis for the patentability of living organisms under the European Patent Convention (EPC) and European Union law will be discussed first. Then will be discussed the specific legal and practical problems that may arise when patenting various living organisms. In addition, the scope of protection afforded to patents on such subject-matter will be analysed.

The Legal Framework

The two relevant sources of patent law in Europe are the EPC and the Biotechnology Directive.[1] The Biotechnology Directive has been incorporated into the EPC.[2] For the purposes of this article, the provisions of the EPC and its interpretation by the EPO Boards of Appeal will be discussed first, while the provisions of the Biotechnology Directive (including the EPC Rules incorporating it) will be considered separately. These are discussed in turn below.

The European Patent Convention

General requirements for patentability

Under the EPC, the requirements for patentability are that the invention be novel, involve an inventive step, have an industrial application and not be excluded from patentability.[3] The claims contained in the application must be clear and supported by the description, while the technical disclosure must be enabling so as to make the invention workable by a third party.[4] These requirements are, in the field of biotechnology, complex and have resulted in much legal writing. For the purposes of this publication, only the requirements that are most problematic for patents on living organisms will be considered, these being mainly exclusion from patentability, enablement and clarity.

Microbiological inventions

Article 53 EPC provides that:

> "European patents shall not be granted in respect of:
> . . .
>
> (b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision does not apply to microbiological processes or the products thereof."

In T356/93 it was confirmed that on a proper construction of that Article, the exclusion from patentability for animal and plant varieties contained in Article 53(b) EPC does not apply to microbiological processes and their products. It was further held that, as a result, micro-organisms could be patentable, being the products of microbiological processes, and were defined as "generally unicellular organisms with dimensions beneath the limits of vision which can be propagated and manipulated in a laboratory" which did include viruses and plasmids.[5] It would thus appear that any unicellular organism of such dimension would be considered a micro-organism for the purpose of patentability and would be patentable even if it were a cell derived from a higher multicellular organism[6] (other authors have suggested alternative definitions taking into account more biological and phylogenic considerations when

[1] Directive 98/44/EC on the legal protection of biotechnological inventions (the "Biotechnology Directive").
[2] The Biotechnology Directive has been incorporated into the EPC by Rule 23b(1) EPC. In addition, Rules 23b–23e EPC expressly restate parts of the Biotechnology Directive.
[3] Articles 52 and 53 EPC.
[4] Articles 83 and 84 EPC.
[5] Plasmids are circular loops of DNA which are part of the genome of bacteria and the most common vector for artificial DNA used by molecular biologists. Plasmids can hardly be classified as living but can nonetheless be replicated in bacteria.
[6] T356/93.

classifying living organisms within the microbiological realm for the purposes of patentability[7]).

While cells derived from a multicellular organism are a patentable product of microbiological processes and patentable as such, whole multicellular organisms regenerated from the multiplication and differentiation of these cells (as happens during cloning) are not considered products of microbiological processes irrespective of whether they are obtained through genetic engineering.[8]

Essentially biological processes

Article 53(b) EPC provides that "essentially biological processes for the production of plants or animals" are not patentable. This presumably was intended simply to prevent the patenting of natural reproductive processes or non-technical processes such as selective breeding.[9] Beyond the patentability of biological processes, this may affect the protection of organisms as such that could be the direct products of such processes.[10]

In T320/87, it was decided that in order to ascertain whether a process for the production of plants or animals was essentially biological, it was necessary to consider the totality of the human intervention and its impact. In addition, a process which comprises at least one essential technical step, which cannot be carried out without human intervention and which has a decisive impact on the final result, is not essentially biological.[11] As a result, the transgenic modification of a living organism by genetic engineering was not an essentially biological process[12] and thus is not barred from patentability on this specific ground.

Plant and animal varieties

The EPC provides for the exclusion from patentability of plant and animal varieties.[13] This has been defined for plants in T356/93 as:

> "any plant grouping within a single botanical taxon of the lowest-known rank which, irrespective of whether it would be eligible for protection under the UPOV Convention, is characterised by at least one single transmissible characteristic distinguishing it from other plant groupings and which is sufficiently homogeneous and stable in its relevant characteristics."

It must be stressed that a taxon, unlike a species, is not a true biological classification. A species is generally defined as a group of living organisms which are capable of sexual reproduction with each other. In other words, although they are all genetically different, they can exchange genetic material with each other as part of their life cycle and have offspring. Such a definition is quite certain and practicable when dealing with sexual reproduction. However, it will break down for living organisms which are capable of asexual reproduction (such as micro-organisms, certain plants and, exceptionally, animals).

A variety is, then, within a species, a subset of individuals which are grouped according to their phenotypic or genetic similarities. No absolute criteria exist and any grouping has to be arbitrary.

For the purposes of the EPC, an unstable plant hybrid will not constitute a variety,[14] while initial case law indicated that transgenic plants had to be regarded as unpatentable varieties.[15] This latter finding has now been overruled in the decision G1/98 where it was finally recognised that a transgenic plant was a patentable embodiment of an invention (i.e. the idea and possibility of specific genetic engineering), provided that plant varieties were not individually claimed as such (even though a patent claim may in fact encompass plant varieties).

The position for animals is markedly different as the non-existence of variety rights for animals has resulted in the diverging interpretation of nearly identical EPC provisions.[16] In T19/90 and V6/92 it was held that transgenic animals were patentable. The reasoning was that such patent claims were not directed to animal varieties but to rodents and mammals which form a taxonomical unit higher than any variety. Furthermore, there was no other form of protection available for animal varieties, unlike that for plants.

"Ordre public" and morality

Article 53(a) EPC provides that patents shall not be granted in respect of inventions the publication or exploitation of which would be contrary to "ordre public" or morality. This Article has been used to oppose patents on transgenic plants and animals. While this has been recognised as a valid objection, it has not been held to exclude transgenic organisms in general from patentability.[17]

---

[7] "TRIPs and the Patentability of Micro-organisms", Dr Mike Adcock and Dr Margaret Llewelyn [2000/2001] 3 BSLR p 91.

[8] T356/93 and G1/98 which dealt with plant cells only. The corresponding case law on the subject of animal cells has not conclusively dealt with this issue (see T19/90 and V6/92).

[9] T356/93.

[10] The direct products of a patented process are protected: Article 64(2) EPC and Article 8(2) of the Biotechnology Directive.

[11] T356/93.

[12] T356/93 for plants and T19/90 for animals.

[13] Article 53(b) EPC.

[14] T320/87.

[15] T356/93.

[16] Variety rights exist only for plants and the preliminary works for the EPC indicated that the legislators sought to ensure that the patent rights and varieties rights did not overlap (see T320/87).

[17] See T356/93, T19/90 and V6/92. In a decision under appeal, the Opposition Division has ruled that transgenic animals designed to develop cancer and used for research would be excluded from patentability under Article 53(a) EPC, if the animals claimed were not test animals in accordance with the laws of the EPC member states: OJEPO 10/2003, page 473.

The Biotechnology Directive: Patentability and the Extent of Patent Protection

The scope of a patent is decided under the terms of the EPC, while infringement is judged solely in terms of national law.[18] The Biotechnology Directive has effects in national law and is incorporated in the EPC.[19]

The Biotechnology Directive therefore affects patentability at EU and national levels, together with the extent of national protection. It also restates part of the provisions of the EPC, presumably to ensure uniformity of national patent law regimes.

Its effects on patentability and on the national protection afforded to patents will be considered below.

Patentability

(1) Microbiological inventions

The Biotechnology Directive expressly states that microbiological processes and products thereof are not excluded from patentability by the prohibition on the patenting of essentially biological processes.[20] This provision incorporates the interpretation of the EPO with respect to similar provisions of the EPC.[21] Rule 23c EPC, implementing parts of the Biotechnology Directive, however, further states that the product of a microbiological process shall not be patentable if it is a plant or animal variety.[22]

(2) Essentially biological processes

The Biotechnology Directive has repeated the bar contained in the EPC on patenting "essentially biological processes for the production of plants or animals".[23]

However, it has gone further by stating that:

> "a process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection".[24]

This definition is, however, different from that which arose from the EPO through case law, as discussed in the previous sections.

The definition of the Biotechnology Directive will bar from patentability only processes which are solely made up of natural steps such as crossing or selection,[25] while the case law of the EPO could bar from patentability a process which contains a non-natural step but which would not be sufficient to have a decisive impact on the final product.[26]

This bar is therefore narrower than that of the EPC as stated in case law and is line with the general purpose of the Biotechnology Directive to promote biotechnology patents and thus prevent national legal systems from construing the EPC narrowly so as to extend the scope of the exemptions from patentability.

(3) Plant and animal varieties

The Biotechnology Directive has not sought to modify the bar on the patentability of plant and animal varieties.[27]

Rather, it has attempted to clarify the issues by stating that:

> "Inventions which concern plants or animals shall be patentable if the technical feasibility of the invention is not confined to a particular plant or animal variety."[28]

A definition of "plant varieties" was incorporated by reference to an EC Regulation which provides that a plant variety is:

> "a plant grouping within a single botanical taxon of the lowest known rank, which grouping, irrespective of whether the conditions for the grant of a plant variety right are fully met, can be:
>
> - defined by the expression of the characteristics that results from a given genotype or combination of genotypes,
>
> - distinguished from any other plant grouping by the expression of at least one of the said characteristics, and
>
> - considered as a unit with regard to its suitability for being propagated unchanged".[29]

As for the previously discussed definition of T356/93, such definition does not constitute a true objective biological definition of a variety. However, it is supplemented by the statements made in the Recitals that:

> "a plant grouping which is characterised by a particular gene (and not its whole genome) is not covered by the protection of new varieties and is

[18] Article 64(3) EPC, confirmed by G2/88.
[19] Directive 98/44/EC on the legal protection of biotechnological inventions, which is incorporated into the EPC by Rule 23b(1) EPC.
[20] Article 4(3) of the Biotechnology Directive.
[21] Notably in T356/93.
[22] This Rule may contradict the interpretation of Article 53(b) EPC as stated in T356/93 and T19/90 but is consistent with G1/98.
[23] Article 4(1)(b) of the Biotechnology Directive.
[24] *ibid.* Article 2(2).
[25] A further difficulty is to determine as a point of construction whether the natural phenomena are limited *ejusdem generis* by the use of the words "crossing or selection".
[26] As was required in T356/93.
[27] As expressly stated in Recital 29 of the Biotechnology Directive.
[28] *ibid*. Article 4(2).
[29] Article 2(3) of the Biotechnology Directive, referring to EC Regulation 2100/94. Rule 23b(4) EPC restates that definition.

> therefore not excluded from patentability even if it comprises new varieties of plants".[30]

While a variety is further defined by:

> "its whole genome and therefore possesses individuality and is clearly distinguishable from other varieties".[31]

Taken together, these should allow for the patentability of an invention which consists of a discrete genetic modification to a plant (or presumably to an animal[32]). Such genetic engineering is not likely to be confined to a particular variety within a species of plants and should be applicable to all plants within a species.[33]

Such modification of a single gene is to be contrasted with the modifications to an entire genome which occur in the creation of a new variety (see Recitals 30 and 31 of the Biotechnology Directive). The former can be defined, disclosed and reproduced easily whereas the latter is to be regarded as a chance event which may not be reproducible (although it may be propagated from a sample).

(4) "Ordre public" and morality

Article 6 of the Biotechnology Directive provides that the following will be considered contrary to "ordre public" or morality and thus not patentable:

> "(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."

The corresponding EPC Rule states that it is not possible to patent inventions which *concern* these four groups of techniques.[34] It must be noted that such wording may be wider in scope than that of the Biotechnology Directive.

(5) Deposition

Under the EPC, it is possible to deposit biological material as a means of helping with the disclosure requirement when patenting an invention that involves the use of or concerns biological material.[35]

Similarly, under the Biotechnology Directive, if an invention involves the use of or concerns biological material which is not available to the public and cannot be enabled by description, then deposition is required.[36] This does not modify the previous position. It must be noted that such requirement is not limited to micro-organisms and could be extended to plants or animals.[37] In practice, however, it is possible to deposit plant cells which can be used to reconstitute the plant or frozen animal embryos. Most biotechnological inventions having as their subject-matter plants or animals would likely be the products of transgenic methods and it should be sufficient to deposit, as DNA, the genetic constructs used for the modification.

Protection

The previous section dealt with the issues of formal patentability. This section will deal with the extent of patent protection available pursuant to the Biotechnology Directive.

(1) Article 8 of the Biotechnology Directive

Article 8 of the Biotechnology Directive provides that:

> "1. The protection conferred by a patent on a biological material possessing specific characteristics as a result of the invention shall extend to any biological material derived from that biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics.
>
> 2. The protection conferred by a patent on a process that enables a biological material to be produced possessing specific characteristics as a result of the invention shall extend to biological material directly obtained through that process and to any other biological material derived from the directly obtained biological material through propagation or multiplication in an identical or divergent form and possessing those same characteristics."

The second paragraph of this Article provides for the protection of biological products obtained from a process producing biological material possessing certain characteristics. The obtainment can either be direct[38] or

---

[30] Recital 31 of the Biotechnology Directive.
[31] *ibid.* Recital 30.
[32] Recital 31 of the Biotechnology Directive only mentions plants, which may result from the fact that at the time when the Biotechnology Directive was drafted, the main difficulties were with the patentability of transgenic plants under the EPC but not with transgenic animals.
[33] Conversely, Recital 32 of the Biotechnology Directive restates that if the genetic engineering is confined to a particular plant variety and a new variety is bred, it will be excluded from patentability.
[34] Rule 23d EPC.
[35] Rule 28(1) EPC.
[36] Article 13 of the Biotechnology Directive.
[37] The definition of "biological material" in the Biotechnology Directive is any material containing genetic information and capable of reproducing itself or being reproduced in a biological system, which would include multicellular organisms: see Article 2(1)(a) of the Biotechnology Directive.
[38] This is the normal position under Article 64(2) of the EPC, but the concept of direct product can be very restrictive in national law, as shown by the following rulings of English courts based on an authoritative examination of European doctrine: *Pioneer Electronics Capital Inc. v Warner Music Manufacturing Europe GmbH* [1995] RPC

through propagation or multiplication (whether in identical or divergent form).

This would apply whenever the biological material product of the patented process (which could be a plasmid or an entire organism) is replicated and for as long as the specific characteristics resulting from the process patent are maintained and recognisable. The purpose of this paragraph would have been to extend the scope of the protection of the products of patented processes. It must be stressed that this would not make these products patentable as such under the EPC.[39]

On the other hand, the first paragraph of this Article appears to extend product patent protection to other biological material derived from the patented product through propagation or multiplication in an identical or divergent form, *provided* that the specific characteristics which were the *result* of the invention are still present.

For the purposes of Article 8(1) of the Biotechnology Directive, the invention is presumably a product invention (as Article 8(2) deals with process inventions). Strictly, a product invention does not confer any characteristics on any product (unlike a process). However, it is submitted that what is meant in this context is that the specific characteristics which must be transmitted for the protection to extend are those which characterise the product invention of which a given biological product is an *embodiment*.

As an example, if an invention were a bacterium resistant to a given antibiotic and producing a given protein, then the specific characteristics which will confer patent protection, if transmitted, are the resistance to the said antibiotic and the production of the given protein.

Such construction is more difficult when dealing with a whole range of characteristics, some being poorly defined or unknown, such as would arise if the product patent were for a new bacterium with a host of useful properties (as opposed to a genetically engineered strain where all the modifications are known). In such a case, it is submitted that the specific characteristics to be taken into consideration are those which solve the technical problem underlying the invention.[40]

For instance, if a patent is obtained following the discovery of a bacterium which is capable of degrading chemical X, and although such organism may have many unknown properties, if the patent is obtained based on solving the problem of degrading chemical X (as forming the basis for the inventive step and for the required specific industrial applicability[41]), then the specific characteristic which will confer patent protection if transmitted in the course of propagation or multiplication is the ability to degrade chemical X.

Although both paragraphs of Article 8 of the Biotechnology Directive make reference to undefined terms such as propagation or multiplication in an identical or divergent form, it is reasonably clear that the extra protection conferred by this Article will only attach to organisms (or biological material) derived from the initial ones through reproduction of a sort (whether natural or not). There is, however, no requirement that the organism (or the biological material) remains unchanged following that process (merely that the specific characteristics are conserved and passed on).

(2) Article 9 of the Biotechnology Directive

Article 9 of the Biotechnology Directive provides that:

> "The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1), in which the product . . . [is] incorporated and in which the genetic information is contained and performs its function."

This Article envisages the patenting of a genetic sequence (either on its own or as a component of a transgenic organism) and its subsequent incorporation in another organism (which can occur through natural reproduction). The protection would then extend to all organisms incorporating the relevant sequence and in which it performs its function.[42]

An effect of this Article is that even if a transgenic organism were not patentable as such (for instance, because of problems with the exclusion of varieties) then, provided that the transgenes[43] used to modify it are patentable as DNA sequences, the organism would be protected.

A problematic feature of this Article could be that a patent on a cloned gene sequence[44] could be construed as conferring protection on any organism carrying a similar

487 and *Pioneer Electronics Capital Inc. v Warner Music Manufacturing Europe GmbH* [1997] RPC 757.

[39] While direct products may be protected by national law under Article 64(2) EPC, they are not as such automatically patentable. See T248/85 and T150/82.

[40] As ascertained by the problem and solution approach. See "The Patentability and Protection of DNA-based Inventions in the EPO and the European Union", Dr Denis Schertenleib [2003] 3 EIPR p 125, for a discussion of its use in molecular biology and the cases T20/81, T1/80 and T939/92, among many.

[41] For a discussion of the concept of specific industrial applicability and utility, see "The Patentability and Protection of DNA-based Inventions in the EPO and the European Union" *supra*; the decision of the Opposition Division published in the EPO's *Official Journal* 6/2002, p 293; the Trilateral Project B3b: Comparative study on biotechnology patent practices, Theme: Nucleic acid molecule-related inventions whose functions are inferred based on homology search; and the Trilateral Project 24.1: Biotechnology comparative study on biotechnology patent practices; which can both be found at www.european-patent-office.org/tws/twsindex.htm.

[42] In itself deciding the real function of a gene is very difficult, but it is possible that, for a finding that such function is performed for the purpose of Article 9 of the Biotechnology Directive, transcriptional activity followed by translation into functional proteins is sufficient.

[43] Transgenes are artificial DNA constructs used for genetic engineering.

[44] A cloned gene or DNA sequence is a fragment of DNA, isolated from the genome of an organism and which is replicated in a bacterial culture.

version of that gene, even if the sequence is naturally present in its genome and not genetically engineered into it. It is, however, submitted that "incorporated" within the meaning of this Article, only refers to incorporation by technical means.[45]

An alternative effect of this Article would be to protect a plant or animal obtained from cells that are patented, as such cells contain genetic information, are incorporated in the resultant multicellular organism and their genetic information would perform its function (assuming that such function does not have to be expressly disclosed in the patent).

Viruses and Bacteria

Now there will be considered the patentability, the possible extent of certain types of patent claims and the protection of viruses and bacteria as a result of both the EPC and the Biotechnology Directive.

Patentability

Viruses and bacteria are patentable *per se*, as the products of microbiological processes. As explained in T356/93, the bar on the patentability of animal and plant varieties does not apply to micro-organisms. Such micro-organisms are therefore patentable under the normal principles of the EPC.

Such micro-organisms are, however, different from other inventions as they are self-replicating and susceptible to mutations and evolution.

Because of their complexity, it is unlikely that a patent could disclose their whole structure, properties and behaviour. As a result, this may cause difficulties for the assessment of novelty, clarity, enablement and eventually infringement.

Formally, such difficulties are alleviated by the possibility of disclosure by deposition which postpones the characterisation work until required, by making samples available to third parties at all times.

The Extent of Allowable Claims

In this section, the problem that will be discussed is the situation where a micro-organism has been isolated and a patent application is made in respect of elements of it (such as with the hepatitis C virus or the AIDS virus).

The question would be whether components of it can be claimed and, more specifically, what threshold of characterisation is necessary for such claims to be enabled and have specific industrial applicability. In the *Chiron NANBV* case,[46] genes belonging to hepatitis C viruses were claimed, but had not all been cloned. It is a valid point to ascertain whether, once a virus has been isolated, one could claim for any uses, all genes of that virus, or of other strains of the same virus.

It is possible to delineate three broad levels of disclosure, which are as follows.

Genes cloned, sequenced and disclosed

This envisages the situation where, in addition to discovering the micro-organism, the applicant has cloned its genome and has sequenced and disclosed all of it. In such a case, provided that the components of the genome that are claimed have a specific industrial applicability and their uses are enabled, there would be no fundamental difficulties in claiming these components of the micro-organism as DNA sequences or proteins (subject always to all the usual requirements of novelty, inventiveness and clarity[47]).

Genes cloned and disclosed as a library

This envisages the situation where the applicant has cloned the genes in a library[48] and has deposited it, but has not identified or sequenced the various clones. Such an approach was taken in the *Chiron NANBV* case where 77% of the genome of a strain of hepatitis C virus had been cloned and sequenced, but where the remaining genes encompassed by the claims had been cloned for that strain but not sequenced and disclosed.[49]

In such a case the difficulty in claiming all these genes is that they are not identified or isolated at that stage and therefore it is difficult to give an enabling disclosure of these or to ensure that they meet the relevant criteria for patentability, including specific industrial applicability. Furthermore, there would be difficulties with the clarity of claims to DNA fragments that are not structurally defined by their sequence but rather contained in a bacterial culture.

It is possible to overcome these objections if isolating further clones from such libraries does not constitute an undue burden (because a clear method for isolation is disclosed) and these have specific industrial applicability (which would require a credible statement of potential uses beyond mere speculation[50]). As an example, if a virus is isolated and its genetic components are cloned and disclosed as a library, it should be possible to claim

[45] See "The Patentability and Protection of DNA-based Inventions in the EPO and the European Union", *supra*.

[46] T188/97.

[47] For a discussion of the effects of these requirements on inventions based on genetic sequences, see "The Patentability and Protection of DNA-based Inventions in the EPO and the European Union", *supra.*

[48] Such libraries are bacterial cultures containing fragments of DNA; what sequences are present is often not known.

[49] T188/97.

[50] Trilateral Projects 24.1 and B3b on homology, *supra*; see footnote 41.

genes coding for proteins that can be used in a detection process, provided that a clear way to isolate the relevant ones is disclosed.[51]

Genes not cloned

In such a case the micro-organism would have been isolated, but not its genes.

The problems with claiming its genetic components are as above, but the issue of the undue burden required to isolate the genes would be more serious. It would be difficult to enable the isolation or the use of these DNA sequences, comply with the requirement of clarity and show a specific industrial applicability if they have not been cloned.

Such a cloning exercise could even be viewed as the product of further research and thus as a "reach-through claim" which ought to fail if the product is not structurally defined.[52]

The Extent of Patent Protection

Similarities between genomes

Patent protection requires the legal assessment of infringement. Yet there is an inherent difficulty in judging whether two organisms are the same for the purpose of infringement. It is, however, now conceivable to sequence the genome of such micro-organisms in order to determine whether they are of the same strain (in other words, whether they have a recent common ancestor).

However, unless they have identical genomes (which is unlikely), two questions will arise: firstly, if these belong to two similar strains and have diverged from an unpatented ancestral form, would one infringe a patent on the other; and secondly, if one strain has evolved or mutated from a patented strain, would it infringe the corresponding patent?

Before the Biotechnology Directive, the answer would have depended solely on the interpretation of the patent claim to the micro-organism (more specifically, whether it would expressly include other strains sharing the characteristics used to define the patented strain) and the use of national doctrines of equivalents which are still not fully developed for such biotechnology patents.[53]

The Biotechnology Directive supplements these general considerations about patent infringement. Of relevance to this issue is Article 8 which was discussed in the previous sections. A reasonable interpretation of its wording would provide for the protection of a strain possessing the specific characteristics which solve the technical problem underlying the invention, *provided* that it was derived from the patented strain through propagation or multiplication.

Therefore the answer to the first question, dealing with separate strains, will depend mainly on the use of the doctrine of equivalents, while the second question, dealing with a derived strain, is within the ambit of Article 8 of the Biotechnology Directive.

In addition, if a relevant characteristic were the product of genetic engineering, then pursuant to Article 9 of the Biotechnology Directive any derived strains bearing the modification would be protected, provided that the transgene responsible for the modification was patented.

The interplay between patents on micro-organisms and patents on their genetic material

Another important question concerns the interplay between a patent on a micro-organism and a patent on its genetic constituents.

Such a situation would practically arise if one patented a micro-organism relying on a useful property and a subsequent worker attempted to use part of that micro-organism's genome (potentially the individual genes responsible for the useful characteristic).

Classically, the result would depend on whether the patent is held to include the genetic constituents of the micro-organism (especially if the dispute revolves around the genes responsible for the useful properties) and of the use of the doctrine of equivalents (any host of the genes cloned could be deemed to be an equivalent of the original micro-organism).

In any event, now as a result of the Biotechnology Directive, any organism carrying a component of the patented micro-organism (i.e. a gene) could be held to infringe the patent on the original organism as a result of either Article 9 of the Biotechnology Directive (provided that such a situation is held to constitute an incorporation of the original organism) or Article 8 (provided that such situation is held to constitute "propagation or multiplication" of the original organism).

---

[51] In the *Chiron NANBV* case (T188/97) it was held that a claim to the DNA sequences of the hepatitis C virus was enabled (as the isolation of further clones from a library or from other strains was technically straightforward, albeit time consuming) but not a claim to antigenic fragments of the corresponding proteins as it was difficult to isolate and recognise these antigens.

[52] Report on comparative study on biotechnology patent practices carried out under Trilateral Project B3b, Theme: Comparative study on "reach-through claims", which indicates that patent claims should at least structurally define the compounds claimed in order to be allowed. The full text can be found at www.european-patent-office.org/tws/twsindex.htm.

[53] See *Kirin-Amgen Inc. v Roche Diagnostics GmbH* [2002] RPC 1 and *Kirin-Amgen Inc. v Transkaryotic Therapies Inc.* [2003] RPC 3, where the issues revolved around a single gene.

The opposite situation would arise where one patented the genetic constituent of a micro-organism. The question would then be whether this patent would protect the micro-organism itself. Under national law it may be that using the micro-organism would be held to infringe the patent on its genes, as one needs to use the genes in order to use the micro-organism.[54] In addition, Article 9 of the Biotechnology Directive could extend the protection from the genes to the micro-organism itself (provided that the genes are deemed to be incorporated into that micro-organism for the purpose of Article 9).

Cell Lines and Stem Cells

Patentability

Cells, even those derived from a multicellular plant or animal, are the products of microbiological processes for the purposes of patentability and thus cell lines are patentable as such.[55]

The Biotechnology Directive provides that the human body and the simple discovery of one of its elements cannot constitute patentable inventions;[56] however, when isolated by technical means the same elements can be patentable.[57] In fact, all cell cultures and cell lines need to be isolated by technical means and as a result this prohibition does not affect the patentability of human-derived cell lines.

In these respects cell cultures do not differ from the microbiological products discussed previously. However, the nature of cell lines and their uses result in difficulties which would not arise with bacteria or viruses. This is due to the fact that each member of a multicellular species has a different genome but has similar or "equivalent" cell types.[58] Similarly, all cell types within a multicellular organism are different but have identical genomes. This can lead to difficulties with the definition and characterisation of the claimed cell lines.

If, however, the purpose of a cell line is merely the production of a defined protein, such as with hybridomas, these problems would be alleviated as the distinguishing characteristic of these cells is the production of a specified protein which can be detected biochemically or sequenced.[59] Patent claims can thus be drafted to be specific to that protein and claim any cell line producing it.

In contrast, cell lines such as a stem cell line are more problematic since their distinguishing effect is their ability to differentiate into other cell types and since all cell lines taken or produced from the same organism have identical genomes regardless of their phenotypic differences.

It is therefore not possible to sequence their genome in order to measure how similar or dissimilar these are. Reliance on functional characteristics and the expression of certain genetic markers can be superficial and the only quantitative way to differentiate them would be to measure their gene expression profile, a task which is still extremely difficult.[60]

Another approach could be to define a cell line not through its intrinsic characteristics but rather through the process of its creation (or isolation), if a specific and reproducible process is known for its production. Such a claim would be termed a product-by-process claim as it would claim a product defined by a process. However, according to the case law of the EPO, it would be acceptable only if the process feature of the claim were necessary and the product were in itself patentable.[61]

An additional problem specific to human embryonic cells is that the Opposition Division of the EPO, in a decision under appeal, has recently ruled that the morality exclusion of Article 53(a) EPC, as interpreted in the light of Article 6 of the Biotechnology Directive and Rule 23d EPC, results in the prohibition of patents on stem cell lines derived from human embryos.[62]

The reasoning of the Opposition Division is based on the premise that the exclusion stated in Rule 23d EPC must be given a wide interpretation, thus extending the exclusion of "uses of human embryos for industrial or commercial purposes" to embryonic cell lines as such and to their uses.

The reason given for such a wide interpretation is that Article 6 of the Biotechnology Directive, interpreted narrowly, would be redundant with Article 5(1). It should be noted that it is arguable that, firstly, Article 5(1) of the Biotechnology Directive should be considered jointly with Article 5(2) which limits its scope and that, secondly, Article 5(1) is concerned with the patentability of elements of the human body (possibly *in situ*) while

[54] In *Merrell Dow Pharmaceuticals Inc v H N Norton & Co Ltd* [1996] RPC 76 it was held that when a pharmaceutical compound was converted in the human body into an active derivative, even if that derivative is unknown, it will be considered as being used for the purposes of novelty. Similarly it could be considered that using a micro-organism involves using its genes.

[55] T356/93: however, the plants that can be regenerated from these cell cultures are not products of microbiological processes for the purpose of patentability.

[56] Article 5(1) of the Biotechnology Directive.

[57] *ibid*. Article 5(2).

[58] For instance two skeletal muscle cell lines from two individuals are genetically different but are "equivalent" as they perform similar functions in similar organisms.

[59] Furthermore, the genome of hybridomas is in fact different from that of the organism from which they are derived because such immune cells modify some of their genes to produce a vast variety of antibodies.

[60] Although, the use of gene chips or similar mass screening methods may make it practicable to define a cell type or a cell line by its gene expression profile. It may be that eventually cell types can uniquely be specified by a set of numbers representing the expression levels of each of their genes.

[61] See T219/83; T320/87 for plants; and T130/90 for hybridoma cell cultures.

[62] Decision of the Opposition Division dated 21 July 2003 on the opposition to patent EP695351.

Article 6 could be construed as dealing solely with processes utilising human embryos.

The Extent of Patent Protection

Cell lines

The extent of patent protection available for a cell line will be dependent on the definition used and the construction of the claims.

Practically, the relevant questions would be in what circumstances two cell lines would be deemed distinct for the purpose of infringement, and what the effect of them being obtained from different donors would be, considering that they may be "equivalent" cell lines.

There would be two possible interpretations: firstly, to confine the patent strictly to the cell line initially isolated and deposited. Such a patent would only protect cells propagated from that cell culture. Such an interpretation would lead to patent rights which would be more akin to a proprietary right *in rem*.

Secondly, to construe the patent as extending to all cells from any similar sources (i.e. from the same species) having the relevant characteristics claimed in the patent. Such interpretation will lead to difficulties in assessing whether a given cell line belongs or not to the protected class. However, it is likely to be a necessary construction as cell lines such as stem cells often need to be derived from the organism in which they are to have a therapeutic effect.[63] As a result, it is necessary to protect all "equivalent" cell lines derived from any possible donors, otherwise the patent protection would be of very limited value.

In the final analysis, this will be an issue of what is deemed to be proportionate with respect to the contribution to the art. It must be stressed that under a product patent, a patented cell line would be protected in respect of any use unless a restriction is contained in the claims or is implied.

However, if the cell line is obtained through genetic engineering this would constitute a discrete genetic invention and would most likely be protected under Article 9 of the Biotechnology Directive and more generally under normal patent protection principles as the modification can be completely disclosed and defined. As a result, any cell line bearing the transgene used would be protected.

An alternative problem would arise if the cell line were defined with a product-by-process claim (such as by stating the method of its isolation or obtention). The question would then be whether such a claim extends to any cell line having the relevant disclosed characteristics or only to these being produced by the process.[64]

If the definition is based solely on a process, then practically in order to show infringement one must show equivalence of process. It would not matter that theoretically one could obtain the same cells through a different process if practically the only evidential mean of ascertaining infringement is by examining the process of production.

If, on the other hand, the process imparts characteristics which can be measured independently of the process, then these will form the evidential basis of any assessment of infringement.

Organisms regenerated from cell lines

It is possible for both plants and certain animals to be regenerated from cell cultures. The resultant multicellular organisms would not be patentable as products of microbiological processes.[65]

However, under Articles 8 and 9 of the Biotechnology Directive, if the cell line from which they are derived is patented, then the protection may extend to the organisms incorporating these cells and regenerated from them.

Plants

Patentability

Transgenic plants

Following the decision G1/98, it would appear that transgenic plants are now patentable. This is confirmed by the Biotechnology Directive, provided that the technical feasibility of the invention is not confined to a particular variety.[66] The concept of variety is still difficult to define (especially in the case of plants reproducing asexually where arguably every individual could be regarded as a variety or a species) and depends on an arbitrary classification.

The Biotechnology Directive clearly indicates that plants bearing a genetic modification to a single gene are patentable.[67] Logically, plants bearing multiple gene modifications also ought to be patentable as they are obtained through of a series of disclosed discrete modifications that are each patentable (which is to be contrasted with a new variety which is made up of a multitude of genetic variations unknown and

[63] Stem cells are of particular interest for transplantation and often must be derived from the host organism to avoid immune rejection.

[64] Such a problem arose in respect of recombinant proteins in the *Kirin v Roche* and *Kirin v TKT* cases at footnote 53 above and illustrated the difficulty in interpreting the extent of product-by-process patent claims.

[65] See footnote 8 above.

[66] Article 4(2) of the Biotechnology Directive.

[67] *ibid*. Recital 31.

undisclosed). Most transgenic modifications will be workable with all varieties within a species and should therefore be patentable.

If the genetic modification only operates in what is defined as a variety or in an individual,[68] then, pursuant to Recital 31 of the Biotechnology Directive, such an invention could be patentable but, following Recital 29, Recital 32 and Article 4(2) will not be patentable as its feasibility is confined to a variety. This is understandable as the effects would not be the products of the invention (i.e. the idea to perform specific genetic engineering) but rather whatever chance event or unknown interaction is in fact responsible for the distinguishing effects.

Novel plants

A different problem would arise if an unknown plant were discovered and had surprising properties.[69] It may be wondered if it would be patentable as such, as would a micro-organism with useful properties. Apart from the question of whether such an organism is novel (i.e. whether it was available to the public before its "discovery") and inventive (whether it would have surprising properties which can form the basis for inventiveness), the main problem would be whether it is barred from patentability as a plant variety. Arguably, if it is truly an unknown species (and not an unknown variety of a known species) then the bar on the patentability of varieties should not apply. On the other hand, the reasoning in T356/93 could exclude such species from patentability as they could meet the definitional requirement of plant varieties. G1/98 would not overturn this finding as it dealt with discrete genetic engineering, nor would the Biotechnology Directive as it rejects inventions that are confined to varieties. Such a situation would test the limits of the patentability of multicellular organisms.

The Extent of Patent Protection

Patent protection on a plant will most likely require an engineered genetic modification. The question of patent protection is therefore that of the extent of protection afforded by the incorporation of a transgene.

Under Article 9 of the Biotechnology Directive, a patent on a transgene incorporated in a plant (or possibly a patent on a cell culture from which a plant is derived) would protect the plant in itself and all others derived from it, provided that the relevant genetic information is traceable. Similarly, under Article 8 of the Biotechnology Directive, a patent protecting a plant (or protecting a process producing a plant) will extend its protection to other plants derived from that plant through breeding or reproduction, provided that the specific characteristics remain recognisable.

Animals

Patentability

The bar on the patenting of animal varieties has been rarely tested, unlike the corresponding one on plant varieties. As a consequence, the law is relatively clearer. In T19/90 and V6/92 (the *"onco mouse"* case) it was held that a patent claiming mammals being genetically engineered to carry additional genes making them susceptible to cancer was valid and not barred by Article 53(b) EPC.[70]

The position arrived at in the *onco-mouse* case should not have been modified by the Biotechnology Directive. Although Recital 31 of the Biotechnology Directive only refers to plants, it should be clear that transgenic animals are not animal varieties.[71]

However, as stated before, it is possible for a given transgenic modification to have different effects according to the variety within a species in which it is introduced (this has been known to happen with the transgenic modification of different rodent strains). In such a case, the invention is feasible only in a single variety. Depending on the interpretation of Article 4(2) of the Biotechnology Directive this may not be patentable. However, if such a transgenic animal has useful properties, it may be reasonable to have protection in place for it (especially as, unlike for plants, there are no corresponding variety rights). In addition, the fact that a biotechnological invention may have a more limited scope of possible embodiments should not be a bar to its patentability.

The question as to whether a true animal variety would be patentable has never been fully assessed through case law, nor has the meaning of "varieties" in animals been defined fully for the purposes of the EPC. Although sexual reproduction with long generation gaps makes it more difficult to produce a true animal variety (although intense inbreeding can), cloning now enables the duplication of all the genetic characteristics of a single individual. If an individual mammal were to exhibit some useful properties, it could be cloned into as many individuals as required. This could be classified as a pure variety. Such an invention can be propagated but cannot

[68] There have been cases where it was found that a genetic modification produced different effects according to the strain of mice used. Although this is unusual, it is possible for genetic engineering to be variety-dependent or to produce results that cannot be reproduced in other individuals.

[69] There has been instances where ancient plants and animals have been re-grown from seeds and eggs; see "Les Inventions Biotechnologiques : la Voie Étroite de la Brevetabilité", M. R. Hirsch & G. Mortreux, *La Gazette du Palais*, 23 January 1999, p 129.

[70] Although it may be barred by Article 53(a) EPC if the genetic modification results in suffering for the animal without substantial medical benefit: see Article 6(2)(d) of the Biotechnology Directive and footnote 17.

[71] See the decision of the Opposition Division, published in the EPO's *Official Journal* 10/2003, p 473.

be applied to any other animals within the same species. Pursuant to the Biotechnology Directive, such a group of animals should be an invention which is confined to a single variety (as it cannot be extended to different animals). It would therefore appear that this would be an unpatentable animal variety.

As for plants, the question of whether a lost or unknown animal species could be patentable is still open, as discussed in the previous sections.

The Extent of Patent Protection

In the case of a discrete genetic modification, such genetic engineering can easily be defined by the presence of a DNA sequence and testing for it would be straightforward. As a result, there is no practical problem with the assessment of infringement of discrete and defined genetic modifications.

As discussed for plants in the previous section, under Article 9 of the Biotechnology Directive, a patent on a transgene incorporated in an animal (or possibly a patent on a cell culture from which an animal is derived) would protect the animal in itself and all others derived from it, provided that the relevant genetic information is traceable. Similarly, under Article 8 of the Biotechnology Directive, a patent protecting an animal (or protecting a process producing an animal) will extend its protection to other animals derived from that animal through breeding or reproduction, provided that the specific characteristics remain recognisable.

Issues with the Current Legal Position

Varieties and the Patentability of Transgenic Plants and Animals

The EPC bar on the patentability of varieties based on a taxonomic definition of varieties should evolve in line with the Biotechnology Directive into a feasibility test, namely whether the invention is applicable to a specific variety only. This, however, still requires the definition of a variety.

While the Biotechnology Directive expressly states that plants produced by genetic engineering are patentable (unless the genetic modification is confined to a plant variety), there is no corresponding statement for animal varieties.

The test of applicability to a specific variety is very different from other approaches and could also bar *process* inventions if their applicability is confined to a given variety.[72] This could be justified on the basis that if a genetic modification is only applicable to a variety then it is likely to be inextricably linked with the myriad of unknown genetic characteristics which give the variety its identity. Such an invention can only be used within the context of that variety and is unlikely to be fully defined and enabled. Should the invention concern plants, there would be available plant variety rights. Unfortunately for animals, this would not be so and it may be wondered why such subject-matter should not be properly protected.

In addition, in order to decide whether a modification is applicable to other varieties, it is necessary to have an understanding of what constitutes a variety in the first place. While this concept is to a certain extent defined for plants, it is still broadly undefined for animals.

It is submitted that a possible test to emerge should be whether a given invention can be worked within a substantial part of a species, in which case it ought to be patentable; or conversely whether it is only workable in a given subset of a species, such subset having a genetic configuration characterised by the existence of various genetic polymorphisms[73] in its whole genome (as opposed to a series of known discrete genetic modifications) which form a stable, transmissible and distinct genetic subset of that species, in which case it should not be patentable.

The Extent of Protection under Articles 8 and 9 of the Biotechnology Directive

Article 8 of the Biotechnology Directive has extended the protection afforded by both product and process patents in the field of biotechnology by ensuring that patent protection attaches to the relevant specific characteristics which are transmitted through the reproduction and replication of living organisms.

Article 9 of the Biotechnology Directive seeks to reinforce this, by protecting any organisms incorporating patented biological material and especially genetic sequences. There may be two possibly unforeseen consequences of its wording.

Firstly, this could allow for patent protection to attach to any organisms which have incorporated, even accidentally, the patented genes. This result is hopefully prevented by the operation of Article 10 of the Biotechnology Directive which seeks to limit patent protection when biological material is propagated as part of its normal life cycle.

---

[72] Article 4(2) of the Biotechnology Directive does not restrict itself to product inventions which may consist of plant or animal varieties; rather it refers to any invention, which arguably includes process inventions.

[73] These are naturally occurring variations in genetic sequences.

Secondly, Article 9 of the Biotechnology Directive could conceivably allow for the protection of any organisms which contain genetic sequences which have been patented. In such a situation, a patent for a given gene would protect not only an organism in which such a gene has been incorporated by genetic engineering, but also any organism which carries that gene naturally. An example would be the patenting of the gene and protein for GFP (green fluorescent protein) derived from jellyfish which could extend patent protection to all jellyfish species naturally carrying that gene (or rather only to their industrial uses, if any). However, it is submitted that incorporation within the context of the Biotechnology Directive means incorporation by technical means and cannot be achieved by the natural presence of a DNA sequence in an un-tampered genome.

Cell Lines and Stem Cells

The difficulty with such subject-matter is, firstly, of a technical nature, as defining any cell line is difficult and will rely on deposition and a description of some characteristics of the cells such as the presence of markers.

If the extent of a patent claim were confined to the actual cell line deposited, any issue of infringement would revolve around the question of whether cells are derived from the same culture.

However, if the patent sought to extend to all cells in other organisms having identical characteristics (as would be desirable for stem cells), the question of a means of deciding if a cell line is "equivalent" to another one becomes unavoidable. (Unless these are the direct products of a patented process or are claimed by a product-by-process claim where the process is properly defined.)

In fact, these considerations are merely part of the wider problem of what protection is appropriate for stem cells given the difficulty in defining them and their biomedical importance.

It is submitted that only very distinctive cell lines should be patentable, with strict criteria as to the extent of protection.[74] It is an open question as to whether product claims for such cell lines are appropriate or even practicable in term of the definition of the claims and the assessment of their infringement.[75]

Finally, the recent issue of the exclusion from patentability of human embryonic cells based on issues of morality has far-reaching consequences for biomedical research. The reasoning of the Opposition Division, based on the premise that the exclusion stated in Rule 23d EPC and Article 6 of the Biotechnology Directive must be given a wide interpretation, should be carefully examined.

It is a general principle that exclusions from patentability should be construed narrowly.[76] While these provisions could conceivably prevent patents being granted on processes using human embryos, these should not lightly be interpreted as barring from patentability cells derived from human embryos or the uses of such cells.

Conclusion

The Biotechnology Directive and its incorporation into the EPC have now created a new and important source of law in the field of biotechnology patent law, which is distinct from both national and EPO case law. It affects the patentability of biotechnologies at the level of the EPC and in national legal systems. It also creates a new set of rules at the level of EU member states for biotechnology patent protection and the assessment of infringement.

Yet it has not been implemented by all members of the EU and there is already a risk of differing implementations across the European Union.[77]

The importance of the legal protection of biotechnological inventions, together with the monopoly risks arising from excessive protection and conversely the damage to commercial research resulting from insufficient protection, require that such a directive be implemented properly and uniformly.

Such uniformity can seldom be achieved by recourse to separate national jurisdictions and it is submitted that the creation of a community patent and its corresponding judicial jurisdictions, able to rule on infringement, is a necessity in order to achieve the biotechnological development that is expected across the enlarging European Union.

[74] The European Group on Ethics in Science and New Technologies to the European Commission has expressed legal concerns over the patentability of stem cells; see "Ethical Aspects of Patenting Inventions Involving Human Stem Cells" n 16, 7 May 2002, which can be found at www.europa.eu.int/comm/european_group_ethics/docs/avis16_en.pdf.

[75] See the statement of the European Group on Life Sciences of November 2001 which can be found at www.europa.eu.int/comm/research/life-sciences/egls/patenting_sta_en.html; "Gene patents: a different approach" [2001] 11 EIPR p 505, Philippe Jacobs and Geertrui Van Overwalle; "Gene and compound per se claims: an appropriate reward?" [2000/2001] 6 BSLR p 239, Alan W. White; and "The Patentability and Protection of DNA-based Inventions in the EPO and the European Union", *supra*.

[76] See T356/93, T320/87 and T19/90.

[77] See "La Directive Européenne sur la Biotechnologie : La Brevetabilité des Séquences Génétiques", Dr Denis Schertenleib, *Décideurs Stratégie Finance Droit*, n°50 2003, p 82.