European Perspective

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This article sets out the European position on patenting life forms which is complicated somewhat by provisions in the European Patent Convention.

In Europe we face many of the same issues in patenting biotechnology as are faced elsewhere, notably the United States, but we also face some special problems of our own making. These special problems arise because of certain express exclusions included in the European Patent Convention (EPC), when it was finalized back in 1973, long before biotechnology was developed. These express exclusions are reflected in the national patent laws of all Western European countries (and an increasing number of Eastern European ones), all of which their laws on the EPC.

One can identify three types of which are covered in this article:

- the 'product of nature' problem, which, however, is not unique to European patent law, and to which the approach in Europe is broadly similar to that in the USA;

and two other types of issue which are an especial feature of European patent law:

- the 'variety' problem;

- the 'ethical' problem, or more accurately problems.

Another exclusion from patentability that is met in Europe, but not in the USA, is methods of medical treatment, but is not directly relevant to the protection of biotechnology, except when one considers certain types of gene therapy.

All three types of issue have been addressed to a degree by the EC Biotechnology Directive, the first version of which started life in 1988,[1] but was rejected by the European Parliament in 1995. It was resuscitated in amended form, is now in force [2] and must be implemented in national patent legislation by Member States by July 2000. However, many of the benefits, in terms of harmonization, that it was hoped that the measure would deliver over a decade ago, when introduced, have now already largely been achieved through a succession of decisions of the European Patent Office (EPO), a fact recognized by the EPO in recently amending its rules to accord with the Directive using a quasi-administrative procedure that is only open to it on the basis that it is declaratory of the EPC.

Thus on 15 June 1999, the EPO Administrative Council accepted a recommendation from the EPO to implement the Directive in European patent law by means of amendments to the EPC Implementing Regulations. The amendments take effect from 1 September 1999 and introduce a new chapter to the Regulations – Chapter VI, on Biotechnological

Inventions (Rules 23b to 23e) grouping definitions and rules of interpretation to be applied to European patents and patent applications which concern biotechnological inventions. The new Rules provide that the Directive 'shall be used as supplementary means of interpretation' (which will mean that its recitals can be taken into account) and reflect the provisions of Chapter I of the Directive, as to which the EPO notes that:

'Although the principles set forth there regarding the patentability of biotechnological inventions are based on the relevant provisions of the EPC and essentially reflect current practice as developed by the Office and its boards of appeal in applying the Convention, some extensions and clarifications are required in this area to ensure that the patentability provisions of the EPC also continue to be interpreted in keeping with the Directive.'

How the Directive deals with the three types of issue identified above is discussed below, although it should be recognized that the Directive also addresses other aspects of biotechnology patenting.

Despite these three specific issues, one should emphasize that much biotechnology is patented in Europe without especial difficulty, for example new techniques which assist in undertaking genetic manipulation. However, when one moves into the area of patenting the *products* of biotechnology, rather than just *processes* by which those products are obtained, a unique combination of problems arises.

The 'product of nature' problem

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

Moreover, by Article 52(2) EPC, certain specified types of subject-matter, one of which is 'discoveries', are not to be regarded as inventions within the meaning of Article 52(1). The four attacks implicit in this formulation of patentability – lack of novelty, inventive step, industrial applicability (or utility), or of being a mere discovery – can all arise when one deals with materials which can to some extent be said already to exist in nature, as do the 'first generation' products of biotechnology.

This 'product of nature' problem, or problems, is one that is not, however, unique to biotechnology and means have already been established to deal with it in other technical fields.

Two of these grounds of attack, lack of novelty and being a discovery, have been addressed in the biotechnology field by the Opposition Division of the EPO in *HOWARD FLOREY INSTITUTE/ Relaxin*[3] claims to DNA fragments encoding for a certain form of the human hormone Relaxin were upheld. These did not lack novelty by virtue of the hormone and the gene always having been present in the human body, as it is an established principle of European patent law to recognize novelty for a natural substance which has been isolated for the first time and which has had no previously recognized

existence, which was the case here.[4] Moreover, the isolation and characterization of such a DNA fragment did not represent a mere discovery, such as finding something freely available in nature, for example a new animal found in some remote region.[5] The applicable principles have long been set out in the EPO Guidelines:

'To find a substance freely occurring in nature is also mere discovery and therefore unpatentable. However, if a substance found in nature in nature has first to be isolated from its surroundings and a process for obtaining it is developed, that process is patentable. Moreover, if the substance can be properly characterized either by its structure, by the process by which is obtained or by other parameters and its is 'new' in the absolute sense of having no previously recognized existence, then the substance *per se* may be patentable. An example of such a case is that of a new substance which is discovered as being produces by a microorganism.'

The inventive step hurdle, better known as the attack of obviousness, has been one which has featured strongly in biotechnology litigation in the UK, the national jurisdiction is Europe with most experience of such matters. Thus in *Genentech Inc's Patent*[6] claim to an already known, isolated and characterized protein, when produced by means of recombinant DNA technology, was held by the English Court of Appeal to lack inventive step as no more that a statement of what was an obvious research goal. Being the first to achieve that goal through the use of conventional techniques did not therefore merit a patent. Similar views were also voiced by the English Court of Appeal in *Biogen v Medeva,* [7] although the patent here was found invalid on the ground of insufficiency, the main claims being too broad given the nature of the contribution to the art (almost a separate problem in its own right for biotechnology patents, at least the early ones). In contrast, in *Chiron Corporation v Organon Teknika*[8] an obviousness attack on validity failed against the first to identify, isolate and characterize, after many years of failed attempts, the virus responsible for most cases of non-A non-B hepatitis, namely hepatitis C.

The utility (or 'industrial application') hurdle, although a subject of controversy, has been less the subject of case law. Once again, the principle, from other fields of technology, is well established. Thus one cannot patent a new chemical unless it has some use – say as a drug, as a lubricant or an intermediate, even though such utility does not form part of the claim unless the claim is in second or subsequent use form. The application of the principle in biotechnology can be most clearly seen in relation to the attempts made both in the USA and Europe in attempting to patent gene sequences of unknown utility. These can be contrasted with the *Relaxin* case, where the utility of the gene sequence, as coding for a specific hormone, was known. In contrast, it seems generally to be accepted that one cannot patent gene sequences of wholly unknown utility, which is how the expressed sequence tag (EST) issue has traditionally been presented.

However, gene sequences are rarely of wholly unknown utility and even where they are, the low utility threshold for patentability might be met by 'use as a probe'. However, if that is so then such gene sequences will be obvious, as the utility is obvious and the means of determining them obvious.

Article 3 of the EC Biotechnology Directive (and corresponding Recital 20 and 21) explains how, in general terms, the principles in Article 52 EPC are to be applied in the case of 'biological material', which is itself, by Article 2.1(a) of the Directive, narrowly defined concept extending to cell lines and genes (which are already regularly patented in Europe) but one which, for example, does not extend to proteins:

'3.1 For the purposes of this Directive, inventions which are new, which involve an inventive step, and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.

3.2 Biological material which is isolated from its natural environment or produced by means of a technical process may be subject of an invention even if it previously occurred in nature.'

'2.1(a) "Biological material" means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system.'

These principles, which are effectively declaratory of existing interpretations of Article 52, are further refined in relation to biological material found in the human body, by Article 5 of the Directive (and the corresponding Recitals 22 to 25):

'5.1 The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

5.2 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.

5.3 The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application.'

As with Article 3, these principles can effectively be seen as no more than declaratory of existing European law, but it is helpful to have them.

But one should keep the 'product of nature' problem in perspective. In the future, once the initial stages of the human genome project have been concluded and as biotechnology comes more and more to involve improving on nature, rather than replicating it, such issues will be become less significant.

The 'variety' problem

Article 53(b) EPC prevents patents being granted for: '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'.

This provision, though not found in US patent law, is permitted for the time being under Article 27(3)(b) of TRIPs, was originally intended to exclude the results of conventional plant breeding activities and can also be protected by another intellectual property right, the plant variety right. As it is the one exception in European patent law which comes closest to being a restriction on 'patenting life' it is important to emphasize the original reason for its existence – to prevent overlap of intellectual property rights.

At first sight it would appear to exclude from patentability genetically altered crops or transgenic animals. However, in *CIBA-GEIGY/Propagating Material*[9] *and LUBRIZOL /Hybrid Plants*[10] a narrow construction was put on the exclusion which in effect overcame the problem. This was followed in *HARVARD/Oncomouse*[11] in relation to animals, [12] where the subject of the main claims was not a single variety, but rather an entire species. Indeed the widest claims went even further, extending to any non-human mammal.

Early in 1995, however, in *PGS/Glutamine synthesase inhibitors*, [13] this principle was undermined, with claims rejected to plants *per se* on the basis that such claims *embraced* plant varieties.

Five years later, during which time the continued prosecution of European patent applications with claims to plants and to animals has been suspended, this case has been shown to have been an aberration and the law put back on the right track by the decision of the EPO Enlarged Board of Appeal in *NOVARTIS II/Transgenic plant*[14] on 20 December 1999.

Even before this decision, the EC Biotechnology Directive took a position contrary to that in *PGS*.
Uncontroversially, Articles 2 and 4 of the Directive (and corresponding Recitals 29 to 33) provide:

'4.1 The following shall not be patentable:
(a) plant and animal varieties
(b) essentially biological procedures for the breeding of plants or animals'

'2.2 A process for the production of plants or animals is essentially biological if it consists entirely of natural phenomena such as crossing or selection.'

Apart from the useful definition in Article 2.2, this is little more than a rearrangement of the words of Article 53(b) EPC. However, Article 4.2 of the Directive continued, in contrast to *PGS:* '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'.

Article 2(3) of the Directive defined 'plant variety' by Article 5 of the Community Plant Variety Rights Regulation[15] which states: '5.2… "variety" shall be taken to mean a plant grouping within a single botanical taxon of the lowest known rank…'. A similar position has now been taken by the Enlarged Board of Appeal in *NOVARTIS*, effectively reversing the reasoning in *PGS*. The Enlarged Board has held, *inter alia* : 'A claim wherein specific plant varieties are not individually claimed is not excluded from patentability under Article 53(b) EPC, even though it may embrace plant varieties'. The Enlarged Board noted that 'in the absence of the identification of specific varieties in the product claims, the subject-matter of the claimed invention is neither limited nor even directed to a variety or varieties' and that 'the exclusion in Art 53(b) EPC was made to serve the purpose of excluding from patentability subject-matter which is eligible for protection under the plant breeders' rights system'.

By incorporating the EC Biotechnology Directive into the EPC by the quasi-administrative procedure that they used in the middle of 1999, the EPO had of course rather assumed that the Enlarged Board would decline to follow the much criticized decision in *PGS*. It has now been saved the embarrassment which would have been caused had it not done so, because the Directive, though it must be implemented by Member States, has no direct effect on the EPC, and independent and freestanding international Convention, which can only otherwise be amended through formal procedures involving a diplomatic conference.

Ethical problems

Article 53(a) EPC prevents the grant of patents for: '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'. To show how standards of 'morality' change, a similar principal was implied by common law in the United Kingdom and was once the basis for rejecting patents for contraceptives. But times change, and Article 53(a) has been pressed into service as a basis for attacking biotechnology patents. It is not, however, the basis of one single attack. Instead, the arguments advanced in support of such an attack are many and varied, such as:

- in relation to the human body, it confers rights of 'ownership' over the body;
- in relation to transgenic animals, it might involve cruelty to such animals;
- it risks damaging the environment.

The latter two objections are less to the principle of patenting than to the underlying work the results of which it is sought to patent. Indeed they each relate to areas where such underlying work is already to a large extent to the subject of regulation. But each of these objections is based on a fundamental misconception as to what patents are about. Thus, in relation to each of these three objections it should be emphasized that the owner of a

patent is not thereby granted a positive right to do something – instead a patent provides a limited right, for 20 years, to stop others doing certain things *commercially*, and other than for *experiment* relating to the subject-matter of the patented invention.

To prevent, as these critics seek to do, a patent being granted because one does not agree with the underlying work it protects is not to deal with the root of the problem that such critics have with biotechnology. Why, therefore, should such considerations have any place in patent law, as opposed to *regulatory* law? Surely the patent office is not the correct forum in which to discuss such ethical matters? Moreover, when such critics advance their objections, who is there to speak for and to represent the wider public interest that in many cases exist – that of the patients, and especially those with genetically-based diseases.

However, in cases such as *HARVARD/Oncomouse,*[16] the EPO has been forced to consider the question and has established certain guidelines, involving weighing possible suffering of animals and risks to the environment, on the one hand, against the invention's usefulness to mankind on the other. In *HOWARD FLOREY INSTITUTE/Relaxin*[17] and *PGS/Glutamine synthesase inhibitors,* [18] Article 53(a) objections have failed. In the latter case the objections were mainly of an environmental nature. In the former case, the objection was a generalized one as to 'the alleged intrinsic immorality of patenting human genes'. As the Opposition Division observed:

'It cannot be overemphasized that patents covering DNA encoding human H2 relaxin, or any other human gene, do not confer on their proprietors any rights whatever to individual human beings… No woman is affected in any way by the present patent – she is free to live her life as she wishes and has exactly the same rights to self determination as had before the patent was granted.'

It is ironic that these ethical questions have not been faced head on, but rather, and then only in an indirect way, through the patent system, which has suffered from being, at least so far, the only forum in which such objections can be advances. These battles should not be fought by proxy in the patent system.

It is to be hoped that the EC Biotechnology Directive, by giving specific examples of activities regarded as in breach of Article 53(a), will take these battles out of the EPO. Article 6.1 of the Directive (corresponding to which are Recitals 36 to 39, 43 and 44) starts by restating Article 53(a), with the omission of the 'publication' wording (which must in any event be deleted form the EPC as being inconsistent with TRIPs):

'6.1 Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.'

Article 6.2 of the Directive (corresponding to which are Recitals 40 to 42 and 45) goes on to provide a non-exhaustive list of examples of material that is unpatentable on this public policy or morality ground. The non-exhaustive nature of the list is also emphasized

by Recital 38, which also gives as an example of a process 'the use of which offends against human dignity,… processed to produce chimeras from germ cells or totipotent cells of humans and animals…', which process is not one of those specifically listed in Article 6.2:

'6.2 On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:
(a) processes for cloning human beings;
(b) processes for modifying the germ line genetic identity of human beings;
(c) use 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 expression 'cloning human beings' in (a) (Recitals 40 and 41) replaces the term 'human reproductive cloning' in an earlier draft, which latter term is generally taken to mean the production of genetically identical human beings,[19] but can be distinguished, for example, from what the Human Genetics Advisory Commission (HGAC) in the UK call 'therapeutic cloning' and which term the HGAC use to describe 'other applications of nuclear replacement technology, which do not involve the creation of genetically identical individuals'.[20] Presumably the wording in the final version of the Directive is meant more clearly to make this differentiation.

By (b) (Recital 40) somatic gene therapy is (at least from this point of view[21]) regarded as patentable. Paragraph (c) (Recital 42) replaces that in the amended draft which excluded 'methods in which human embryos are used'. Paragraph (d) (Recital 45) is declaratory of the law as established by the EPO in the infamous *Oncomouse* case which found that a mouse with a genetic predisposition to cancer and which was a useful test animal for cancer research was patentable.

Article 7 is a somewhat curious declaratory statement: 'The Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology'. It may also serve to provide another basis for taking the discussion of ethical issues away from the patent system. If it succeeds in so doing this innocuous little provision may prove to be one of the most important contributions made by the Directive to biotechnology patenting in Europe.