PATENTING DNA SEQUENCES

by Ewan Townsend, Stephanie Hutchinson and Christopher Stothers

Introduction

In recent years, improvements in automated gene analysis techniques and computer power have led to the rapid accumulation of genetic code information. Biotech companies compete to file patent applications primarily to secure protection for the DNA sequences of the genes they have identified. However, obtaining patents for DNA sequences generally requires more than the identification of the sequence.

The number of cases challenging the validity of patents for DNA sequences indicates the commercial importance of this issue. Patents, if valid, give the owner the exclusive right to prevent others from manufacutring and selling products which use the patented sequence. Competitors with pipeline products need to know whether they are free to market their new product without falling within the scope of a valid patent.

This article considers the approaches taken in the UK, Europe and the United States towards patents claiming DNA sequences, and provides some practical guidance for innovators involved in patenting DNA sequences.

Patentability of DNA sequences in Europe

It is not currently possible to obtain a European Union-wide patent. However, the European Patent Convention (EPC) provides a centralised framework for the grant of national patents throughout Europe via the European Patent Office (EPO). The EPO has considered the patentability of DNA sequences on various occasions, as have national courts which enforce patents and can revisit the issue of validity.

The key European legislation is set out in the EPC and the Biotechnology Directive (the Directive)[1]. The Directive confirms that biotechnology inventions are patentable and provides further guidance on the interpretation of the requirements set out in the EPC.

EWAN TOWNSEND, STEPHANIE HUTCHINSON and CHRISTOPHER STOTHERS are specialists in patent law at Arnold & Porter (UK) LLP, London

Correspondence: Christopher.Stothers@aporter.com

Article 5 of the Directive states (with emphasis added):

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

It is therefore clear that an isolated or technically-produced *"sequence or partial sequence of a gene"* is potentially patentable. The main stumbling block in attempts to patent DNA sequences in Europe has been demonstrating the "industrial application" of such a sequence. This requirement has been interpreted differently in the EPO and by the UK courts.

Approach of the EPO

The EPO approaches "industrial application" on a case-by-case basis. However, whilst emphasizing that each case must be decided on its own facts, it has provided guidance in a number of cases and is generally considered to take a broader, more flexible approach than some national courts. It construes the notion of industry broadly[2] considering how a skilled reader would interpret the patent with the benefit of his own common general knowledge.[3]

For example, in one recent case the EPO found that the disclosure of *"a real possibility of exploitation"* of the sequence in question was sufficient.[4] In another, it was prepared to acknowledge a "*possible function* [of a protein encoded by a patented DNA sequence] *based on computer-assisted methods*".[5]

Approach of the UK courts

The UK courts impose a significantly higher hurdle and will only recognise

"industrial application" where the patent application discloses the specific function of the protein encoded by the sequence in question. This issue was considered in the recent case of *Eli Lilly and Co. v Human Genome Sciences Inc*[6] (in relation to a patent which had been granted and upheld by the EPO).[7]

Both the trial court and the Court of Appeal held that it was not enough to tell the skilled reader that the protein encoded by a claimed DNA sequence was structurally similar to a known family of proteins and was believed to have similar biological effects and activities. The Court of Appeal summarised its view by stating *"however clever and inventive you may have been in discovering a gene sequence, you cannot have a patent for it or for the protein for which it encodes if you do not disclose how it can be used*[8]". It went on to state that "*discovering a nucleotide sequence encoding for a human protein and being able to show that the protein concerned has some common homology with known proteins (i.e. is a member of a family) may satisfy [the requirement for industrial applicability]. But whether it does or not is case dependent and in particular depends upon how well established the functions of the other members of the family are. To say 'my new protein is similar to a known family of proteins' is not all that helpful in indicating a possible use if the function of that family is itself poorly understood at best.*"[9] The level of disclosure was found to be "*too speculative to provide anything of practical value other than information upon which a research programme could be based*".[10]

The patentee has been granted permission to appeal to the Supreme Court, which will hear the case in July 2011. However, unless the approach is changed by the Supreme Court, the UK courts will continue to require a very specific disclosure of the industrial application of a claimed DNA sequence.

Patentability of DNA sequences in the US

Patents are granted by the United States Patent and Trademark Office (USPTO). Enforcement takes place before the courts, which can also consider challenges to validity.

The position in the United States has been driven by the courts, rather than legislation, and until recently the US courts applied the general principle that "*anything under the sun made by man*" was patentable.[11] Patents on isolated DNA were therefore generally available provided that:

(i) the relevant DNA sequences had been purified and transformed from their natural form by the application of artificial tools; and

(ii) the other statutory requirements had been satisfied, including a requirement that the application disclosed a specific, substantial, and credible utility.[12] This test was similar to, although arguably less stringent than, the requirement for industrial application in Europe.

However, the recent ruling in the *Myriad case*[13] suggests that the US courts may be starting to take a harder line on patent applications claiming DNA sequences. In that case, the US District Court applied a test requiring compositions derived from nature to have "*markedly different characteristics*" from the raw material, requiring that they "*possess a new or distinctive form, quality or property*". However, the case has been appealed to the Court of Appeals for the Federal Circuit, where a range of interventions have been filed. If the case is upheld and followed, applicants may experience difficulties in obtaining patents for isolated DNA sequences unless they can demonstrate that such sequences differ in some way from natural DNA.

Scope of protection

Even where a patent has been granted and is valid, the protection offered is only of practical benefit to innovators if it can be used to keep competing products off the market. Applicants should therefore consider the potential commercial uses of a DNA sequence when applying for patent protection.

For example, in the recent *Monsanto* case,[14] the Court of Justice of the EU held that imported soy meal made from beans carrying the Monsanto's patent-protected DNA sequence did not infringe the patent as the genetic material in the (dead) soy meal was not performing its intended function (ie. confirming herbicide resistance on soy plants). The protection for DNA sequences in Europe therefore appears to be limited to situations in which the genetic material actually exerts its function, rather than extending to any substance derived from or produced by organisms bearing the sequence in question.

Conclusion

There is (and likely always will be) a divergence of opinion as to whether and when DNA sequences should be patentable and how much protection they should give. The approaches taken by national and supra-national court are evolving over time, but for now those involved in patenting DNA sequences are being required to adapt to meet the increasingly stringent requirements for patentability. Innovators may find it helpful to bear the following principles in mind:

- When seeking patent protection for a DNA sequence, consider how it differs from a naturally occurring sequence and what useful application the sequence might have. Do not assume that just because you have identified an interesting sequence you will be able to obtain patent

protection for it. Merely describing the DNA sequence and the protein it encodes with a general idea of its function may not be enough. Although patent filing should be considered as early as possible, failure to consider these points may lead to the application ultimately being rejected.

- In Europe, patents granted by the EPO may face even stricter scrutiny before national courts in the UK and elsewhere, particularly in terms of the identification of possible industrial application[8].
- In the US, it may become necessary to distinguish the characteristics of the sequence claimed from native or natural DNA (e.g. by stressing different chemical or biological properties or by including additional materials or components).
- Even if you are successful in obtaining a patent for your DNA sequence, the scope of protection will not be unlimited. In Europe, for instance, it may only extend to material in which the DNA is actually performing its function.

References

1. Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions [1998] OJ L213/13
2. Case T 0870/04 Max-Planck
3. Case T 604/04 Genentech
4. Case T 18/09 Neutrokine Alpha/Human Genome Sciences, Inc.
5. Case T 641/05 GPCR-like receptor/Pharmacia
6. Eli Lilly and Co. v Human Genome Sciences Inc. [2008] EWHC 1903 (Pat); on appeal, [2010] EWCA Civ 33
7. Case T 18/09 Neutrokine Alpha/Human Genome Sciences, Inc.
8. [2010] EWCA Civ 33, para 57
9. Ibid, para 102
10. Ibid, para 145
11. Diamond v. Chakrabarty, 447 U.S. 202 (1980)
12. See In re Fisher, 421 F. 3d 1365 (Fed. Cir. 2005)
13. Ass'n for Molecular Pathology v U.S. Patent & Trademark Office, 702 F. Supp. 2d 181 (S.D.N.Y. Mar. 29, 2010), appeal docketed, No. 2010-1406 (Fed. Cir. June 22, 2010)
14. Case C428/08 Monsanto Technology LLC v Cefetra BV (EUCJ, 6 July 2010)