# The Validity of Gene Sequence Patents in the UK

Winter 2009

**The High Court Hands Down its Decision in *Eli Lilly v Human Genome Services*[1]**

Whilst data mining, gene sequencing and bioinformatics have become fundamental tools in biotechnology, unless the function of a gene or a protein immediately suggests a practical application further work will be required before an enforceable patent in the UK can be obtained. Due consideration will need to be given to carrying out further investigative research before filing a gene or protein sequence patent.

Human Genome Sciences, Inc (HGS) filed a patent application disclosing the nucleic acid and amino acid sequences of a new member of the TNF superfamily, which they called Neutrokine-α. A European patent was granted but it soon became the subject of opposition p-roceedings at the European Patent Office (EPO). One of the opponents was Eli Lilly & Company. They had been investigating and developing a therapeutic product based upon Neutrokine-α. It has been reported that Eli Lilly have spent some £25m developing an antibody to Neutrokine-α and expect to spend another £125m taking the drug through clinical trials. The Opposition Division of the EPO has recently revoked the patent, which HGS can appeal.

The subject of the proceedings before the High Court was the corresponding UK patent. Eli Lilly could have awaited the outcome of the opposition (and probable appeal) proceedings at the EPO. Revocation of the European patent would invalidate the patent in all contracting states, including the UK. However, it seems that Eli Lilly were in no mood to await the outcome in Europe. They therefore brought revocation proceedings against the patent in the UK.

The principle point of law upon which this decision was based was that the invention was not capable of industrial application. This is a point of law that has rarely come before the English courts.

***Industrial Application***

One of Eli Lilly's main attacks was that HGS failed to properly characterise Neutrokine-α, its function, or any therapeutic or diagnostic utility for it such that it could not have any application in industry. It is a requirement of patentability in Europe that an invention is susceptible of industrial application. This is derived from Articles 52(1) and 57 of the European Patent Convention. These Articles correspond to Sections 1(1)(c) and 4 of the UK Patents Act 1977. The purpose of these provisions is to ensure that an invention has a real world practical application. Whilst this is normally readily apparent (and thus, rarely contested) it is not always the case for biotechnology inventions, especially when the function of protein is not understood.

The Biotechnology Directive (98/44/EC) states that a DNA sequence without an indication of function does not contain any technical information and is therefore not a patentable invention and that the industrial application of a sequence or partial sequence of a gene must be disclosed in the patent application. The Rules of the European Patent Convention also have similar requirements.

Mr Justice Kitchin arrived at the following (abbreviated) principles on industrial applicability:

- The notion of industry must be construed broadly.
- The industrial exploitation must be derivable by the skilled person from the description read with the benefit of the common general knowledge.
- The description must disclose a practical way of exploiting the invention in at least one field of industrial activity.

- There is a need to disclose in definite technical terms the purpose of the invention and how it can be used to solve a given technical problem.
- The requirement will not be satisfied if what is described is merely an interesting research result that might yield a yet-to-be-identified industrial application.
- The purpose of granting a patent is not to reserve an unexplored field of research for the applicant nor to give the patentee unjustified control over others who are actively investigating in that area.
- If a substance is disclosed and its function is essential for human health, then the identification of the substance having that function will immediately suggest a practical application. If, on the other hand, the function of that substance is not known or is incompletely understood, no disease has been identified which is attributable to an excess or a deficiency of it, and no other practical use is suggested for it, then the requirement of industrial applicability is not satisfied.
- Using the claimed invention to find out more about its own activities is not in itself an industrial application.
- It is no bar to patentability that the invention has been found by homology studies using bioinformatics techniques although this may have a bearing on how the skilled person would understand the disclosure.

***Decision***

HGS argued that at the date of filing, members of the TNF ligand superfamily had proved to have industrial applicability and that any skilled person reading the patent would appreciate that both the protein sequence and antibodies raised to it would have the potential for commercial exploitation. However, the Judge was of the view that simply identifying a protein does not necessarily confer industrial utility upon it. This might be so when the identification of the protein immediately suggests a practical application (such as with insulin, human growth hormone and erythropoietin). However, if the function of the protein is not known or is incompletely understood and if no disease has been attributed to a deficiency or excess of it, then the industrial utility must be identified in some other way. Whilst the Judge accepted that Neutrokine-α might be expected to play a role in regulating the activities of B cells and T cells and play an unspecified role in regulating the immune and inflammatory response, he still concluded that this did not reveal how it could be used to solve any particular problem. Accordingly, the patent did not meet the requirement of industrial applicability.

***Additional allegations***

Eli Lilly also alleged that the specification did not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art, and that the invention was obvious to the skilled person. Whilst a detailed discussion of those points is beyond the scope of this article, the Judge held that the sequences and the antibodies were sufficiently disclosed, but that the pharmaceutical and diagnostic composition claims were insufficient. The decision on obviousness was similarly split; the Judge held that the claims were not obvious over an EST and a clone, but that the claims made no contribution to the art because the patent does not teach the person skilled how to solve any technical problem using Neutrokine-α.

**Patentability of Dosage Regime Patents in the UK & Europe Under the Spotlight**

Prior to this Court of Appeal decision, case law in the UK had maintained that a new dosage regime could not impart novelty upon a claim. The opposite was true in Europe. This created the situation where dosage regime claims granted by the EPO were unlikely to be enforceable in the UK. This decision now brings the UK into line with the EPO on dosage regime patents, although the legal situation is still not fully settled.

Until recently, UK and EPO law had differed on the question of whether novelty could reside in a second medical use claim, where the drug is not novel and the indication is not novel, but the dosage regime for that use is novel. It has been settled for some time in Europe that the novelty of such claims can reside in the dosage regime. In contrast, case law in the UK had maintained that such claims were not valid. Accordingly, dosage regime claims granted by the EPO were unlikely to be enforceable in the UK.

In the UK, the Court of Appeal recently held in *Actavis UK v Merck*[2] that in second medical use claims novelty can reside in a new dosage regime of a known substance for a known indication. Whilst this decision goes against established UK case law — such as *Bristol-Myers Squibb v Baker Norton* — it was distinguished on the basis that this earlier decision did not contain a clear rationale that a second medical use claim lacked novelty if the only difference between it and the prior art was a new dosage regime for a known medical condition.

European Patent Office Technical Board of Appeal decision T1020/03 held that there is nothing in the EPC which prevents Swiss-style claims being granted for novel and inventive dosage regimes of an existing medicament.[3] This was the first decision from the EPO in which a pure dosage regime was recognized as not being excluded from patentability. This decision is widely followed by the EPO. More recently, decision T1319/04 concerned a dosage regime patent covered by Article 54(5) EPC 2000 under the transitional provisions. The Board of Appeal did not rule directly on whether whether to grant the patent under the provisions of EPC2000, but instead referred (as Case G2/08) the following questions to the Enlarged Board of Appeal:

1. Where it is already known to use a particular medicament to treat a particular illness, can this known medicament be patented under the provisions of Articles 53(c) and 54(5) of the EPC 2000 for use in a different, new and inventive treatment by therapy of the same illness?
2. If the answer to question 1 is yes, is such patenting also possible where the only novel feature of the treatment is a new and inventive dosage regime?
3. Are any special considerations applicable when interpreting and applying Articles 53(c) and 54(5) of the EPC 2000?

Whilst the Court of Appeal decision brings the UK into line with the EPO on dosage regime patents, some uncertainty still remains. In the UK, Actavis have the possibility to appeal to the House of Lords. In Europe, the decision in G2/08 is awaited with interest.

**House of Lords Revisit Inventive Step – Or is That Inventive Stent?**

This decision from the House of Lords provides a less complicated approach to the assessment of inventive step in the UK and is therefore to be welcomed. When considering this issue it appears that a patent specification should disclose enough information to make the invention plausible rather than having to demonstrate that the invention actually works.

In *Conor Medsystems v. Angiotech Pharmaceuticals*, both the UK High Court and the Court of Appeal revoked Angiotech's patent for lack of inventive step relating to stents coated with Taxol. Stents are used following surgery to enlarge narrowed coronary arteries. The stent prevents re-narrowing of the arteries (restenosis). A common problem with stents is that their insertion can lead to the local proliferation of blood vessel cells (angiogenesis) which can actually cause restenosis. The release of Taxol from the stent was found to inhibit restenosis by preventing angiogenesis. The main reason for the finding of obviousness in the High Court and the Court of Appeal was the lack of any experimental evidence provided in the specification that a Taxol-coated stent actually reduces restenosis.

In the House of Lords,[4] Lord Hoffman did not follow the approach of the lower courts. He stated that there was no requirement when assessing inventive step to actually prove that the invention worked. Whilst the law does require that the patent teach how to make the invention work, this does not form part of the inventive step requirement. According to Lord Hoffmann, the invention should not be determined by "some vague paraphrase based upon the extent of (the patentee's) disclosure in the description."

In deciding what the inventive concept was, Lord Hoffman's approach was to look at the claim since the purpose of the claim is to define the invention. He concluded that the invention was the use of a taxol-coated stent to prevent restenosis. This was not obvious. All that is required to fulfil the inventive step requirement is that the invention will plausibly work, based on the contents of the patent specification (assuming, of course, that the claimed invention, once considered

plausible, is not obvious over the prior art). The Angiotech patent contained data (an angiogenesis-inhibition assay) showing that it was plausible that a Taxol-coated stent would prevent or treat restenosis. Since the prior art did not contain a clear pointer that Taxol could be used in this way, Lord Hoffman concluded that the criterion for inventive step was met.

**Footnotes:**

[1.] *Eli Lilly & Company v. Human Genome Sciences, Inc.*, [2008] EWHC 1903 (Pat.), July 31, 2008, available at: www.bailii.org/form/search_cases.html.

[2.] *Actavis UK Ltd. v. Merck & Co., Inc.*, [2008] EWCA Civ. 444, May 21, 2008, available at: www.bailiii.org/form/search_cases.html.

[3.] EPO Technical Board of Appeal 3.3.4, decision T1020/03, October 29, 2004, available at: http://www.epo.org/patents/appeals/search-decisions.html

[4.] *Conor Medsystems Inc. v. Angiotech Pharmaceuticals, Inc.*, [2008] UKHL 49, July 9, 2008, available at: www.bailiii.org/form/search_cases.html.