UK Supreme Court lowers the threshold for biologics patents

Summary and implications

The UK Supreme Court has handed down an important judgment that establishes when patents for biological materials will satisfy the test of industrial applicability[1].

This judgment will potentially have a strategically significant effect on the position across Europe and in member states of the European Patent Convention ("the EPC").

- This decision is of considerable importance to the research-based biotechnology industry. If a new potentially biologically active protein is discovered a patent can legitimately be applied for it at an early stage of the R&D program. It need not be delayed until the industrial applicability of the protein can be fully demonstrated.
- One of the key new principles is that where the protein is said to be a family or superfamily member, if the disclosure is important to the pharmaceutical industry, the disclosure of the sequences of the protein and its gene may be sufficient, even though its role has not yet been clearly defined.
- As a matter of public policy there is a fine balance between the competing interests of allowing a patentee to have a monopoly over a particular biological molecule too early – which may shut out any competition - and setting the standard for patentability too high (which may negate the incentives of the patent protection system and have a chilling effect on investment in bioscience and innovation).
- The Supreme Court has reiterated that, as far as possible, national patent law in the UK (and across EPC member states) should be interpreted in light of the relevant jurisprudence of the European Patent Office.

The key issue in this case

Article 52(1) EPC provides that an invention must be "susceptible of industrial application" if a European patent is to be obtained for it. Article 57 states that an invention is susceptible of industrial application if it can be made or used in any kind of industry. The primary issue in this case is the way in which this requirement of industrial applicability extends to a patent for biological material.

The Supreme Court and the correct test for industrial applicability for biological material

There is very little UK authority on industrial applicability in the context of biological material. The applicable principles are all to be derived from the EPO jurisprudence. In *HGS v. Eli Lilly* the Supreme Court therefore extensively reviewed and summarised the corpus of relevant EPO case law on industrial applicability in relation to biological material. Given the importance of consistency of interpretative approach between national courts and the EPO - the so-called "dialogue" between a national court and the EPO and between national courts themselves – this careful and detailed analysis will be of central importance across Europe for the foreseeable future.

The Supreme Court held that the "essence" of the EPO jurisprudence on industrial applicability in relation to biological material is as follows.

The general principles are:

(i) The patent must disclose "a practical application" and "some profitable use" for the claimed substance, so that the ensuing monopoly "can be expected [to lead to] some … commercial benefit"[2]

(ii) A "concrete benefit", namely the invention's "use … in industrial practice" must be "derivable

directly from the description", coupled with common general knowledge.[3]

(iii) A merely "speculative" use will not suffice, so "a vague and speculative indication of possible objectives that might or might not be achievable" will not do.[4]

(iv) The patent and common general knowledge must enable the skilled person "to reproduce" or "exploit" the claimed invention without "undue burden", or having to carry out "a research programme".[5]

Where a patent discloses a new protein and its encoding gene:

(v) The patent, when taken with common general knowledge, must demonstrate "a real as opposed to a purely theoretical possibility of exploitation".[6]

(vi) Merely identifying the structure of a protein, without attributing to it a "clear role", or "suggest[ing]" any "practical use" for it, or suggesting "a vague and speculative indication of possible objectives that might be achieved", is not enough.[7]

(vii) The absence of any experimental or wet lab evidence of activity of the claimed protein is not fatal.[8]

(viii) A "plausible" or "reasonably credible" claimed use, or an "educated guess", can suffice.[9]

(ix) Such plausibility can be assisted by being confirmed by "later evidence", although later evidence on its own will not do.[10]

(x) The requirements of a plausible and specific possibility of exploitation can be at the biochemical, the cellular or the biological level.[11]

Where the protein is said to be a family or superfamily member:

(xi) If all known members have a "role in the proliferation, differentiation and/or activation of immune cells" or "function in controlling physiology, development and differentiation of mammalian cells", assigning a similar role to the protein may suffice.[12]

(xii) So "the problem to be solved" in such a case can be "isolating a further member of the [family]".[13]

(xiii) If the disclosure is "important to the pharmaceutical industry", the disclosure of the sequences of the protein and its gene may suffice, even though its role has not "been clearly defined".[14]

(xiv) The position may be different if there is evidence, either in the patent or elsewhere, which calls the claimed role or membership of the family into question.[15]

(xv) The position may also be different if the known members have different activities, although they need not always be "precisely interchangeable in terms of their biological action", and it may be acceptable if "most" of them have a common role.[16]

The Supreme Court's conclusions

The Supreme Court held that the disclosure and existence of Neutrokine-α (and its gene sequence) and its membership of the Tumour Necrosing Factor ligand superfamily, coupled with the common general knowledge, was enough to satisfy the Article 57 test of industrial applicability. It therefore overturned the decisions of the Patents Court and the Court of Appeal, and restored the patent.

It is normally almost unheard of for the UK Supreme Court – or any appellate court for that matter – to disagree with the concurrent findings of specialist judges. But here the case did not involve a re-evaluation of the evidence, but rather of the correct application of the relevant legal principles.

In doing so the Supreme Court strongly criticised Kitchin J's analysis as diverting attention away from points which were likely to lead to a balanced decision, and criticised Jacob LJ as setting a more exacting standard for susceptibility to industrial application than that used by the EPO. Jacob LJ appeared to the Supreme Court to have been looking for a description that showed that a particular use for the product had actually been demonstrated rather than that the product had plausibly been shown to be "usable". The EPO Technical Board of Appeal ("TBA") had – in contrast - regarded the latter as an industrial activity in itself.

Factual background

In 1996 Human Genome Science Limited filed an application for a novel human protein called Neutrokine-α, which was granted by the European Patent Office in 2005. The inventive concept of this patent was the identification of a new member of the TNF ligand superfamily (Neutrokine-α) and the elucidation of its nucleic acid and amino acid sequences.

It is important to note the precise ambit of the invention in this case, as this is critical to understanding the test of industrial applicability established by the Supreme Court's judgment, and the extent to which this has a wider impact across Europe. The patent included the following features:

(i) the existence and amino acid sequence of Neutrokine-α

(ii) the nucleotide sequence of the gene encoding for Neutrokine-α

(iii) the tissue distribution of Neutrokine-α

(iv) the expression of Neutrokine-α by its mRNA (the encoding gene) in T-cell and B-cell lymphomas, and

(v) the information that Neutrokine-α is a member of the TNF ligand superfamily.

The patent also contained contentions as to the biological and potential therapeutic properties of Neutrokine-α and its antibodies. These included that Neutrokine-α would be active in directing the proliferation, differentiation, and migration of T-cells. The gene sequence for Neutrokine-α had been identified using bioinformatics (computational biology) rather than the standard route of a lab-based technique. This meant that the patentee was unable to resolve Neutrokine-α's actual activity.

The first member of the TNF superfamily was TNF-α, which by the patent's application date in 1996 had long been known as a cytokine with a significant role in regulating immune cells. At least eight other members of the superfamily family had also been found (including TNF-β).

Members of this superfamily had various features. Amongst others, all played a role in the regulation of T-cell proliferation and T-cell mediated immune responses, some played a role in inducing cell death, and TNF-α and TNF-β functioned as primary mediators of immune regulation and inflammatory response. However, at the relevant date only TNF-α had been shown to have a therapeutic application (the treatment of rheumatic arthritis).

The problem with the patent – and which led to the present dispute – is that the patent's contentions as to the biological and potential therapeutic properties of Neutrokine-α and its antibodies were all predictions. These were substantially based on the proposition (and no more) that Neutrokine-α is one of the members of the TNF ligand superfamily. In essence the patent appeared to be little more than a claim to an arbitrary member of the TNF ligand superfamily without a known function.

As a general point, once the nucleic acid sequence of a new member of the TNF ligand superfamily becomes available, it is then possible to use well known techniques to express the protein, analyze its structure, develop antibodies, and then make therapeutics and diagnostics for diseases associated with under or over expression of this protein.

In the early 1990s the use of computational bioinformatics enabled researchers to identify genes (and the proteins for which they encode) by comparing their sequences with previously identified and characterised genes. But this did not make it possible to determine – at least, not conclusively – the actual activity of any gene or protein until cloned and subject to *in vitro* and *in vivo* assays.

The dispute

After the patent was granted in 2005 it was opposed in the EPO by Eli Lilly (who was itself conducting an R&D program to commercialise Neutrokine-α), together with parallel UK revocation proceedings.

The central issue in both sets of proceedings was whether, in the light of the common general knowledge at October 1996, by disclosing the facts summarised above (i.e. the existence and structure of Neutrokine-α, the sequence of its encoding DNA, its tissue distribution, its expression, and its membership of the

TNF ligand superfamily), the patent satisfied the EPC test of industrial applicability so that HGS could claim the encoding gene for Neutrokine-α.

The EPO Opposition Division revoked the patent on the basis that the claimed invention constituted no more than a claim to an arbitrary member of the TNF ligand superfamily without a known function. This was overturned by the TBA.

The TBA held that the patent's notional skilled addressee would have appreciated in the light of the common general knowledge of the TNF ligand superfamily and its properties that Neutrokine-α would - as stated by the patent - be "active in directing the proliferation, differentiation, and migration of T-cells". The TBA concluded that "the description of the patent delivers sufficient technical information, namely the effect of Neutrokine-α on T-cells and the tissue distribution of Neutrokine-α mRNA, to satisfy the requirement of disclosing the nature and purpose of the invention and how it can be used in industrial practice." The TBA therefore held that that was a sufficient function to satisfy the test of industrial applicability under Article 57.

Meanwhile in the English revocation proceedings the Patents Court (Mr Justice Kitchin) revoked the patent expressly on the basis of the common general knowledge. He held that that in the light of the common general knowledge the notional addressee of the patent would have concluded that the functions of Neutrokine-α "were, at best, a matter of expectation and then at far too high a level of generality to constitute a sound or concrete basis for anything except a research project". He concluded that simply identifying a protein was not necessarily sufficient to confer industrial utility upon it.

This reasoning was upheld and approved by the Court of Appeal (Lord Justice Jacob) even though by that stage the TBA's decision upholding the patent had been handed down.

The importance of consistency between national courts and the EPO

As a general point the national courts of the EPC member states and the EPO are meant to interpret the EPC in the same way. And in doing so the national courts will pay due deference to reasoned and detailed decisions of the senior courts of other member states (such as the English Court of Appeal and UK Supreme Court), so that as harmonised an approach as possible is followed across EPC member states.

This contrasting set of decisions therefore opened up a distinct gap between the jurisprudence of the UK and the EPO (and potentially of the EPC member states). The jurisprudential problem was whether the Court of Appeal had effectively set too high a standard for industrial applicability in the context of a patent for biological material.

The Supreme Court reiterated the central importance of a commonality of approach between the EPO and the Courts of EPC member states. Both apply the principles contained in the EPC. The Supreme Court stated expressly that it is plainly appropriate in principle, and highly desirable in practice, that all these tribunals interpret the provisions of the EPC in the same way.

The correct approach was that where the TBA has adopted a consistent jurisprudential approach to an issue, it would require very unusual facts to justify a national court not following that approach. When the question is one of principle, uniformity in interpretational approach is desirable so far as possible. National courts are however entitled to come to different conclusions for example where the evidence may be different, and are always entitled to ignore a TBA decision which a national court considers may take the law in an inappropriate direction, misapplies previous EPO jurisprudence, or fails to take a relevant argument into account.

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(Endnotes)

1 Human Genome Sciences Inc v. Eli Lilly & Co [2011] UKSC 51, 2 November 2011

2 BDPI Photophase/Max-Planck T 0870/04, para 4, and Hematopietic receptor/ZymoGenetics T 0898/05, paras 2 and 4).

3 T 0898/05, para 6, and PF4A receptors/Genentech T 0604/04, para 15.

4 T 0870/04, para 21 and T 0898/05, paras 6 and 21.

5 T 0604/04, para 22, T 0898/05, para 6.

6 T 0604/04, para 15, T 0898/05, paras 6, 22 and 31.

7 T 0870/04, paras 6-7, 11, and 21; and T 0898/05, paras 7, 10 and 31.

8 T 0898/05, paras 21 and 31, and Serine protease/Bayer T 1452/06, para 5.

9 Factor 9/John Hopkins T 1329/04, paras 6 and 11, T 0640/04, para 6, T 0898/05, paras 8, 21, 27 and 31, T 1452/06, para 6, and T 1165/06 para 25.

10 T 1329/04, para 12, T 0898/05, para 24, T 1452/06, para 6, and IL-17 related polypeptide/Schering T 1165/06, para 25.

11 T 0898/05 paras 29-30.

12 T 1329/04, para 13, T 0898/05, para 21, T 1165/06, paras 14 and 16, and T 0870/04, para 12.

13 T 1329/04, para 4, T 0604/04, para 22, and T 1165/06, paras 14 and 16.

14 T 0604/04, para 18.

15 T 0898/05 para 24, T 1452/06, para 5.

16 T 0870/04, para 12, T 0604/04, para 16, T 0898/05, para 27.

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