How much for how little?

The Hon Mr Justice Kitchin[1]

For many years the Patents Court in the UK had a reputation for being rather hostile to patentees, particularly in the pharmaceutical sector. But I detect that over the course of the last three years that reputation has melted away. Reports have reached me that recent decisions have "delighted pharmaceutical clients" and that "there has been quite a pro-patent trend in the past year".

Some of these decisions have concerned the scope of patent claims and whether they may be said fairly to reflect the advances actually made by inventors. There can be no doubt this is an important issue in any area of technology. After all, the contemporary justification for a patent system is to encourage innovation and to procure the publication of information about the invention. Moreover, such a system must provide rights which are clear in their scope and relatively easy to enforce. But considerations such as these may be said to afford no justification for a monopoly which extends beyond the scope of the invention and which serves only to inhibit further research and hinder competition.

These are matters which arise acutely in relation to pharmaceuticals and life sciences where new preparative and analytical techniques are constantly evolving. Particular objectives may be entirely obvious but very difficult to achieve; and the potential routes for doing so may be quite unrelated. Is the person who finds one route entitled to a monopoly over all others? Naturally occurring molecules such as proteins and nucleic acids may be assumed to have some useful function for otherwise they would not exist. The problem lies in discovering what they do. Is the person who merely identifies and isolates a new protein entitled to a patent? The isolated protein may be new and non obvious and, if the patentee has disclosed a way of making it, the description may be sufficient. What more does he have to do by way of disclosing a use for it? And if he discloses one use, is he entitled to a monopoly over all uses? If so, his monopoly may be extremely valuable because, as we increasingly recognise, naturally occurring molecules may have multiple functions. But would it be tied adequately to his invention or technical contribution?

In this paper I would like to consider these questions by reference to one case in detail, that of *Lundbeck v Generics*[2] and mention two others of some importance, *Conor v Angiotech* [3]and *Lilly v HGS* [4].

Lundbeck - the facts

[1] A Judge of the High Court, Chancery Division and Senior Judge of the Patents Court
[2] [2007] RPC 729 (Pat); [2008] RPC 437 (CA); [2009] UKHL 12
[3] [2006] RPC 28 (Pat); [2007] EWCA Civ 5 (CA); [2008] UKHL 49
[4] [2008] RPC 29 (Pat)

This action concerned a patent for an anti-depressant drug called escitalopram (branded Cipralex) which was launched by Lundbeck in 2002 and was, at the date of the trial, the world's top selling branded anti-depressant in terms of volume.

Lundbeck is a relatively small research based pharmaceutical company based in Denmark which specialises in diseases of the central nervous system. In the 1970s it synthesised a new compound called citalopram which was found to be a member of the class of drugs called selective serotonin reuptake inhibitors (SSRIs). These drugs selectively inhibit the reuptake of serotonin by nerve cells and so promote neurotransmission. It is this quality which makes them useful for the treatment of depression.

In the late 1980s the first SSRI was launched onto the UK market. It was called fluoxetine (branded Prozac). Others rapidly followed, including paroxetine (branded Seroxat) and citalopram. They have all been very successful. The patent for citalopram expired several years ago and since that time generic versions of the drug have been sold by a number of rival companies.

Citalopram is a racemate and so comprises (+) and (-) enantiomers. By 1988 it was well understood that the vast majority of drugs exert their activity by binding to a protein receptor to form a drug-receptor complex, that the binding site of any drug is in a chiral environment, and that where the drug substance has an asymmetric carbon atom or atoms, the binding efficiency to a given receptor and so also the biological activity of the enantiomers might well be different. It was also generally known that very often the majority of the biological activity observed for a racemate resides within a single enantiomer, although no sure prediction could be made as to whether the enantiomers were equally active or whether one, and if so which, was more active than the other. An inactive enantiomer was considered, at best, ballast but might be toxic or have some other negative effect. Further, by that date the regulators considered that an investigation of the enantiomers was desirable and it was believed that such an investigation might in due course become mandatory. All these matters provided a clear motive to isolate and test the enantiomers. In short, investigation of the enantiomers of citalopram was an obvious goal for the ordinary skilled chemist in 1988.

Nevertheless, resolution of enantiomers was not necessarily a straightforward task. Most resolutions were accomplished through the use of reagents which were themselves optically active. Another technique was to try and develop a chiral synthesis. A yet further technique was to try and resolve a reaction intermediate.

For reasons I shall elaborate, it is also important to have regard to another technology which was emerging at about that time, namely chiral HPLC. A number of publications after the priority date demonstrated that citalopram can in fact be resolved by preparative chiral HPLC. But in 1988 the technique was very much in its infancy and was not something the skilled person would have turned to as a matter of course. It was, however, a fast moving area of research and one which very soon would provide an effective and entirely different way of resolving citalopram.

No doubt acting with the above considerations in mind, from about 1980 scientists at Lundbeck set about resolving the enantiomers of citalopram. They tried a variety of classical techniques using diastereomers, new resolving agents, derivatives and asymmetric synthesis, all without success. Eventually they found two ways which worked, both of which involved resolving an intermediate racemic diol into its enantiomers and then, in a stereoselective way, converting these enantiomers into the corresponding citalopram enantiomers. They found that the activity of citalopram lay entirely in the (+) enantiomer, which they called escitalopram, and, in 1989, they duly applied for the patent in suit.

But Lundbeck did not limit their claims to the methods for making escitalopram which they had discovered and disclosed. Instead:

- Claim 1 was directed to the (+) enantiomer itself, however it might be made;
- Claim 3 was directed to a pharmaceutical composition containing the (+) enantiomer of claim 1;
- Only claim 6 was directed to the particular methods for making the (+) enantiomer which Lundbeck had disclosed.

The attack and findings at trial

The claimants sought revocation of:

- Claims 1 and 3 for lack of novelty in light of the disclosure of the racemate in Lundbeck's patent for citalopram;
- Claims 1, 3 and 6 for obviousness;
- Claims 1 and 3 for insufficiency because they claimed the (+) enantiomer made by any method whereas the specification disclosed only two ways of making it.

At trial, I rejected the allegation of lack of novelty because the citalopram racemate did not fall in the scope of any of the claims. The allegation of obviousness also failed because the particular schemes and techniques which Lundbeck had used to resolve citalopram were not obvious ones to adopt in 1988. However, the allegation of insufficiency succeeded.

The reasoning underpinning the decision in relation insufficiency ran as follows. The decision of the House of Lords in *Biogen v Medeva* [5] and of the Board of Appeal in T409/91 *Fuel Oils/EXXON* [6] permitted an enquiry as to whether the extent of the monopoly, as defined by the claims, corresponded to the technical contribution Lundbeck had made to the art. If a patentee describes a new and non obvious compound which has a beneficial effect and describes a way by which it can be made then he is entitled to a patent for the compound. In such a case the technical contribution lies in the provision of the new and useful compound. Others might find different ways of producing it. But this does not render the original patent insufficient because in each case they are making use

[5] [1997] RPC 1
[6] [1994] OJEPO 653

of the technical contribution – the knowledge they are making the new and useful compound.

However, the same cannot be said of the case where a patentee has found one way of making a compound which was known to be an obvious goal. In the case of citalopram it was entirely obvious that the activity might lie primarily in one enantiomer rather than the other. Further, once the enantiomers had been separated the tests which the inventors carried out to determine where the activity lay were routine and straightforward, as were the steps necessary to formulate the (+) enantiomer into a pharmaceutical composition. The inventive step taken by the inventors of the patent was not deciding to separate the enantiomers of citalopram but finding a way it could be done. In these circumstances the technical contribution they made was the discovery that the diol intermediate could be resolved and then the enantiomers of the diol converted into the enantiomers of citalopram whilst preserving their stereochemistry – and that was all. There was no teaching in the patent as to how that goal could be achieved other than by the use of the diol intermediate. Yet claims 1 and 3 of the Patent covered all ways of making the (+) enantiomer of citalopram. For example, they covered resolving citalopram on a preparative chiral HPLC column – a rapidly developing technology at the date of the patent. Such a method of resolution owed nothing to the teaching of the patent or any principle it disclosed.

In short, the first person to find a way of achieving an obviously desirable goal was not permitted to monopolise every other way of doing so. Claims 1 and 3 were therefore too broad. They extended beyond any technical contribution made by Lundbeck.

Reversal on appeal

The Court of Appeal upheld the findings on the issues of novelty and obviousness but reversed the finding of insufficiency.

Lord Hoffmann explained that in an ordinary product claim, the product is both the invention and the technical contribution. It is sufficiently enabled if the specification and common general knowledge enable the skilled person to make it. One method is enough. There is no justification for distinguishing between product claims depending on whether or not the desirability of making them was obvious. He distinguished *Biogen* as being a case concerned with 'product by process' claims where the product was defined partly by the way it had been made and partly by what it did. The claim limitation thus encompassed a variety of possible processes but the specification only described one. He also drew support from other decisions of the EPO in which an obviousness objection had been rejected where the patent claimed a product which was known to be desirable but previously there was no known way to make it.

Jacob LJ agreed. He considered the point had a short answer. The claim was to the (+) enantiomer. That was novel and non obvious. If one asked the question: "Does the patent enable the skilled man to make it?" the answer was "Yes". So the patent disclosed the invention in a manner sufficiently clear and complete for it to be carried out.

This February, the House of Lords rejected the claimants' appeal. The three principal speeches all had at their heart essentially the same reasoning. Lord Walker explained that *Biogen* was to be distinguished on the basis that the claim, being a product by process claim, had a very large number of possible embodiments. Moreover, he drew a distinction between "the inventive concept" which was the kernel or essence of the invention and the "technical contribution to the art" which was concerned with the evaluation of the inventive concept, or how far forward it had carried the state of the art. In *Biogen* the technical contribution was one way of making the product, whereas in Lundbeck's case it was the provision of the (+) enantiomer.

Lord Mance similarly reasoned *Biogen* was not concerned with a simple product claim and that a product by process claim was different in nature. Moreover the claimants' argument found no support in the statutory language reflecting articles 83 and 84 EPC or in EPO jurisprudence.

Lord Neuberger considered first the statutory language and concluded it did not assist the allegation, there being no suggestion the description did not enable the manufacture of escitalopram. He also considered it highly material the approach contended for was not to be found in any EPO decisions. These matters were sufficient to decide the point against the claimants, subject to the decision in *Biogen*. As to that, the claim in that case was in product by process form and was "at least as much a process claim as a product claim" and so was very different to that in the Lundbeck patent.

Justification for broad claims?

The notion that the extent of a patent monopoly should correspond to the technical contribution to the art in order for it to be supported or justified is a long standing one. It was articulated in 1993 by the Technical Board of Appeal in *Exxon*. But its scope first found full expression in the UK in *Biogen*.

The claim of the patent in issue in *Biogen* was to an artificially constructed molecule of DNA carrying a genetic code which, when introduced into a suitable host cell, would cause that cell to make antigens of the hepatitis B virus ("HBV"). It was drawn in product by process form. In *Lundbeck* at first instance, the facts of *Biogen* were summarised in this way:

> "In 1978, the priority date, it was known that the infective agent responsible for causing hepatitis B was a small particle called the Dane particle consisting of a circular molecule of DNA in a protein core surrounded by a protein surface. It appeared to have at least two antigens, one at its core (HBcAg) and one at its surface (HBsAg). One way of obtaining these antigens was to purify them from Dane particles taken from infected blood. Another promising way to was to use recombinant DNA technology.

> Shortly before the priority date it had been found by a Dr Villa-Komaroff that it was possible to express the DNA for the production of eukaryotic proteins (which those of HBV necessarily were) in prokaryotic bacterial host cells. But those working in the HBV field faced a difficulty which Dr Villa-Komaroff did not. Eukaryotic DNA had been found to contain introns – sequences of DNA that do not code for anything. Eukaryotic cells have a mechanism for stripping out the introns as part of the process by which the DNA is transcribed into mRNA. However it was assumed that prokaryotic cells such as bacteria did not have this mechanism, which meant that they might not be able to transcribe the eukaryotic genomic DNA.
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> One way of addressing this problem was to use artificial cDNA made from mRNA from which the introns had been removed, and this is what Dr Villa-Komaroff had done. But no source of mRNA for HBcAg and HBsAg was available by the priority date. Another way was to sequence the HBV genome, discover where the relevant genes were and see if they did in fact contain introns. However this had not been achieved at the priority date.
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> It was against this background that Professor Murray made the discovery which led to the patent. He purified genomic DNA taken from Dane particles and cut it into the largest possible fragments so as to give himself the best chance of not cutting the relevant genes, and then he inserted these fragments by established techniques into bacterial host cells. The cells produced HBV antigens. This was surprising because, as he put it, genes from eukaryotic organisms would not normally be expressed in bacteria – because of the presence of introns.
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> Some six months after the priority date, the DNA for the Dane particle was sequenced. It was found that the genes which coded for HBsAg and HBsAg did not have introns. Once the sequence became known it was accepted no one would follow the path taken by Professor Murray. Instead, enzymes could be chosen to digest the sites closest to the HBsAg and HBsAg genes and then the fragments of genomic DNA could be inserted into bacterial cells by known techniques and expressed to produce the HBV antigens. Biogen accepted that at this point the invention was obvious."

The key question before the House of Lords was whether the invention was supported by the description of the work carried out by Professor Murray which was contained in the priority document. If it was not, then the patent was not entitled to priority and it would inevitably fall.

Lord Hoffmann affirmed that for matter to be capable of supporting an invention it must contain an enabling disclosure, and that this was also a requirement of sufficiency under article 83 EPC. He then proceeded to elaborate what that meant. He first explained at pages 48-49 that the specification must enable the invention to be performed to the full extent of the monopoly claimed. Importantly, he then accepted that the teaching of the priority document enabled the skilled man to produce both HBcAg and HBsAg in any

cells, and in that sense to produce products across the scope of the claim. But this was not an end of the matter, as he elaborated at pages 50-51:

> "But the fact that the skilled man following the teaching of Biogen 1 would have been able to make HBcAg and HBsAg in bacterial cells, or indeed in any cells, does not conclude the matter. I think that in concentrating upon the question of whether Professor Murray's invention could, so to speak, deliver the goods across the full width of the patent or priority document, the courts and the E.P.O. allowed their attention to be diverted from what seems to me in this particular case the critical issue. It is not whether the claimed invention could deliver the goods, but whether the claims cover other ways in which they might be delivered: ways which owe nothing to the teaching of the patent or any principle which it disclosed.
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> It will be remembered that in Genentech I/Polypeptide expression the Technical Board spoke of the need for the patent to give protection against other ways of achieving the same effect "in a manner which could not have been envisaged without the invention". This shows that there is more than one way in which the breadth of a claim may exceed the technical contribution to the art embodied in the invention. The patent may claim results which it does not enable, such as making a wide class of products when it enables only one of those products and discloses no principle which would enable others to be made. Or it may claim every way of achieving a result when it enables only one way and it is possible to envisage other ways of achieving that result which make no use of the invention."

Applying these principles to the facts of the case, Lord Hoffmann concluded that the claim was indeed too broad, not because it was not possible to produce all the claimed results – indeed, as I have mentioned, that was accepted – but because the same results could be achieved by different means.

The years following 1997 witnessed considerable discussion as to how far the principles explained in *Biogen* extend and, in particular, whether an assessment of insufficiency can involve an enquiry into whether the monopoly encompasses ways in which the invention may be performed which owe nothing to any teaching in the specification. The decisions of the appeal courts in *Lundbeck* have now provided considerable clarification. *Lundbeck* concerned a claim to a single product. Such a claim is sufficient if the specification discloses how to make it. There is no requirement it must disclose more than one way of doing so. That remains the case even if the desirability of making the product was obvious and other ways of making it owe nothing to the invention.

Nevertheless, it may be a useful exercise for commentators to consider the reasoning in *Lundbeck*, not least to assess where the boundaries of each decision lie. It appears to have three core strands. The first, and to my mind most fundamental, is that *Biogen* concerned a product by process claim which defined the products the subject of the monopoly partly by what they did and partly by how they were made – that is to say by recombinant

technology. That expression included a wide variety of processes and yet the priority document only disclosed one.

This distinction itself raises some interesting issues. It must be remembered a product by process claim is still a claim to a product, albeit one which, at least at the date of the patent, the inventor has been unable to define in chemical or in physical terms.[7] So the claim in *Biogen* was not a method claim at all. It was a product claim to recombinant DNA encoding HBcAg and HBsAg, and so by definition to new products. Moreover, and importantly, the House of Lords accepted in that case that the skilled person could produce products across the scope of the claim without undue difficulty. In other words, the House accepted that the specification and the common general knowledge taught at least one way of making all those new products. Now it is true to say that the claim provided an effective monopoly over *all* ways of making those products by recombinant technology but, as will be appreciated, so also did the claim to the (+) enantiomer in *Lundbeck*. Indeed, in a very real sense the claim in *Lundbeck* was more, not less, objectionable, for two reasons. First, the (+) enantiomer was a clear and obviously desirable goal. Secondly, the claim in *Lundbeck* provided a monopoly over *all* ways of getting to that goal, not just a class of ways, such as the recombinant techniques identified in the claim in *Biogen*.

The second strand of reasoning is that there is no support for the objection in the language of articles 83 and 84 EPC. However, it may be noted that Lord Mance himself observed in *Lundbeck* that both the statute and the EPC leave much room for judicial interpretation. Moreover, and as the Board has made clear, the requirement of sufficient disclosure is to ensure that the patent monopoly should be justified by the actual technical contribution to the art[8]. What is the actual technical contribution to the art where an inventor finds one way of achieving an obvious goal? Is it the goal itself, even in a case such as *Lundbeck* where it is clear that rapid technical advances will mean that the technique found by the inventor will soon be superseded, or at least by-passed? Does it truly extend to methods of making an obvious product which owe nothing to anything disclosed by the inventor?

The third strand of reasoning is that there is no EPO jurisprudence supporting the approach of the trial judgment. It is of course highly desirable that the approach of the national courts and that of the EPO should be consistent. But that does not mean to say that in the case of any divergence the national courts are wrong. Furthermore, this is an area in which the jurisprudence has been developing. As the House noted in *Biogen*, it reached a different conclusion to the Board. And in *Lundbeck* both the Court of Appeal and the House of Lords recognised the issue of insufficiency in cases of patents concerning obvious goals has not hitherto been addressed by the EPO.

[7] *Kirin-Amgen* [2005] RPC 169 at paras 88-91

[8] Interestingly, Lord Mance also observed at [45] of his speech in *Lundbeck* that the concepts of inventive step and technical contribution appear to have been treated by Lord Hoffmann in *Biogen* as effectively synonymous.

Observers may detect a degree of tension between the reasoning in *Biogen* and that in *Lundbeck* leading, perhaps, to the conclusion that *Biogen* has no wider application than the facts of that particular case. Accordingly, the only requirement imposed on a patentee is to provide a disclosure which permits his monopoly to be performed across the breadth of the claim; and in the case of a product by process claim that includes the various processes it encompasses. By contrast, a claim to a product *per se* is sufficient if the patent discloses one way of making it, even though the product was known to be desirable and the claim covers all ways of making it, including ways which owe nothing to the invention. As Jacob LJ said, the concept "that the patentee should not have more than he deserves" does not form part of the test.

The issues arising in relation to scope of monopoly and inventive contribution are by no means limited to cases involving obvious goals. In *Conor v Angiotech* the trial judge again revoked a patent on his assessment of the contribution made by the patentee, but this time for obviousness. He was upheld in the Court of Appeal but reversed on further appeal to the House of Lords.

The claims were to a stent coated with a particular anti-angiogenic (anti-proliferative) factor called taxol which acted to inhibit restenosis. Interestingly, as originally drafted the patent's disclosure and claims went much wider and contained very little about restenosis at all. But the patent was extensively amended in the EPO and correspondingly before the Patents Court to limit the claims to stents coated with taxol. The trial judge considered the question of obviousness had to be answered by assessing the contribution to the art disclosed by the specification. He was satisfied that the disclosure was that taxol might be incorporated in a stent but did not suggest that such a stent would be safe or prevent restenosis. In summary, the disclosure was only that taxol should be incorporated in a stent *with a view to seeing whether* it would work and be safe. That much was obvious and so the patent was invalid. It had made no contribution to the art. The Court of Appeal upheld his decision. The patentee had done nothing *by his disclosure* to deserve a monopoly and the information in his patent added nothing to the knowledge of the skilled man.

The House of Lords allowed the appeal. Lord Hoffmann explained that Conor's attack amounted to an illegitimate amalgam of inventiveness and either sufficiency or support. There was enough in the specification to render the claimed invention more than mere speculation. Accordingly, the question was whether it was obvious to use a taxol coated stent to prevent restenosis. Had the judge asked himself this question he would have rejected the obviousness allegation.

What can be concluded from *Conor*? Again, there is no room for the judge to determine the issue of obviousness by reference to his own assessment of the contribution the patentee has made. Provided it is plausible, validity must be determined by reference to the invention found in the claim.

The final case to which I would refer is *Lilly v HGS*. This is a decision of the Patents Court. I ordered revocation of the patent, as did the Opposition Division. Appeals are

pending from both decisions. Briefly, the facts as found at trial were these. HGS had discovered a new protein called Neutrokine-α and identified it as a member of the TNF ligand superfamily. But the identification of the protein did not immediately suggest a use for it and that the specification did not identify any industrial application other than by way of speculation. It required a research programme to identify where the protein was expressed, where its receptors were expressed and what its activities appeared to be. In these circumstances the claimed inventions (in particular the protein and DNA encoding it) were not susceptible of industrial application at the date of the patent and it was no answer to say that subsequent research had shown they might be useful to treat diseases associated with B cell disorders. For like reasons, the claims were invalid for obviousness. They provided no technical contribution and the skilled person was left with a research programme to put the protein to use.

The *Lilly* case therefore provides an illustration of a third way claims may be attacked for undue breadth. To adopt the words of the Supreme Court: "a patent is not a hunting licence. It is not a reward for the search, but compensation for its successful conclusion"[9]. On the facts as found at trial the decision may be considered entirely consistent with *Conor* which recognised that a patent will not be granted for a patent which is mere speculation. But it is not difficult to imagine slightly different circumstances which would again raise some interesting questions. Suppose a new protein is found without invention and it can be made without difficulty by routine expression of the DNA which encodes it, but its functions – which are thought, rightly, to be many and varied – require enormous effort to elucidate. Suppose also that a scientist discovers one of those functions. Is he entitled to a patent for the isolated nucleic acid, the protein it encodes and to a pharmaceutical composition or diagnostic containing that protein? If he is, there can be no doubt that he will have a very valuable monopoly, for it will cover the use of that protein to diagnose or treat any of the diseases associated with all of those functions. But would that be an appropriate reward for his contribution in finding just one of them?

Conclusion

Where does this leave us in the UK? I would summarise it this way. Recent attempts by trial judges in *Lundbeck* and *Conor* to limit the scope of monopolies or deny them altogether in the light of the judges' assessment of the technical contributions made by inventors have not met with favour on appeal. Certainly there is no room to distinguish between goals which are obvious and those which are not. A person who finds a way of making a product which is an obvious goal is entitled to a claim to the product and not just his way of making it. And the first person to make a new product and propose a plausible use for it appears to be in a strong position to contend for a monopoly which covers all uses, whatever the technology. The benefit of this approach is that it provides certainty. But does it do so at the expense of fairness?

[9] *Brenner* 383 US at 535-36