

Patents and enantiomers: the Court of Appeal reflects on Ranbaxy v Warner-Lambert

Dr Brian Whitehead, Stuart Jackson and Richard Kempner of Addleshaw Goddard discuss the latest ruling.

In an earlier article (*Pharmaceutical Law Insight* (Volume 2: December/January) (pp7–10)), the authors considered the decision of the Patents Court in *Ranbaxy UK Ltd & Arrow Generics Ltd v Warner-Lambert Company* [2006] FSR 14. The Court of Appeal has now upheld that decision ([2006] EWCA Civ 876), and in this article the authors seek to analyse its implications for research-based companies and generics manufacturers in the pharmaceuticals sector.

The High Court's decision

Ranbaxy sought a declaration of non-infringement in respect of Warner-Lambert's patent EP(UK) 0247633 ('633), which covers a class of compounds which includes atorvastatin, a cholesterol synthesis inhibitor. The calcium salt of atorvastatin is sold by Pfizer (Warner-Lambert's parent company) as Lipitor and is currently the world's top-selling drug, with global sales in excess of US\$12bn.

In separate actions, which were heard together with the first action, Ranbaxy and Arrow sought to revoke the patent EP(UK) 0409281 ('281), a later patent which specifically claims a single enantiomer of atorvastatin calcium.

Pumfrey J refused the declaration of non-infringement for '633 but held that '281 was invalid for anticipation and obviousness. Ranbaxy obtained leave to appeal on the '633 point, and Warner-Lambert cross-appealed on the '281 point.

The '633 patent

The background chemistry is explained in the earlier article. The '633 patent claims a class of compounds with a given structural formula and a range of substituents. The structural formula in the patent appears to show a single enantiomer (termed the '*R,R* enantiomer') of the claimed range of compounds. However, it was common ground that the method of preparation set out in the patent specification would yield

the racemate (ie a 50:50 mixture of the two enantiomers, *R,R* and *S,S*), rather than a single enantiomer. Ranbaxy proposed to market the single *R,R* enantiomer of atorvastatin calcium. In essence, the issue was whether the claims in the '633 patent could be construed to cover the single *R,R* enantiomer, or whether the patent protected only what was expressly taught – ie the racemate.

Pumfrey J, applying the test set forth by the House of Lords in *Kirin Amgen v Hoechst Marion Roussel Ltd* [2006] EWCA Civ 876, held that although the structural formula showing a single enantiomer was in fact used to denote a racemate (which is common practice among chemists), the skilled man would recognise that:

'... there is a single enantiomer that is the effective compound, and that he can resolve the racemate using conventional techniques in order to extract that enantiomer.'

The claim therefore covered both the racemate and the individual enantiomers, and the declaration of non-infringement was accordingly refused.

In the appeal, Ranbaxy sought to argue that the formula in the patent could represent either the racemate, or a single enantiomer, but not both. Furthermore, as the perception of the skilled man would be that the *S,S* enantiomer is not an active compound, he would form the view that the patentee did not intend to claim the *S,S* enantiomer, and could therefore not have intended to claim the single *R,R* enantiomer either. Had the patentee wished to do so, it could have done so easily by claiming it explicitly. Therefore the patent covers only the racemate.

This argument was rejected by the Court of Appeal. Jacob LJ held that this interpretation was one '*that no rational patentee would have intended*'. According to Jacob LJ, the overriding issue is that the

skilled reader of the patent would know that the *R,R* enantiomer is the form of the drug which has most or all of the pharmaceutical activity. He would expect the patentee to know that too, and would also know that the patent was drafted by someone who knew what its function was. The notion that the skilled man would interpret the claim as excluding the *R,R* enantiomer, because the *S,S* enantiomer would be perceived as inactive '*reeks of an overmeticulous rather than purposive approach [and] flouts technical and business commonsense*'. Accordingly, in the context of the patent, the structural formula denotes both the racemate and/or either enantiomer.

Neuberger LJ explained an additional straightforward reason why the '633 patent covered the *R,R* enantiomer. Although the racemate may be regarded as a different substance from either of the individual enantiomers, it is in fact simply a mixture of the two, and it was a matter of common sense that in the present context, a claim to the racemate was intended to cover each enantiomer of which it was composed.

The '281 patent

Pumfrey J held that '281 was invalid for (i) anticipation by Warner-Lambert's application under PCT number WO 89/07598; and (ii) lack of inventive step over the application for '633. In the earlier article, the authors stated:

'It is submitted that this part of the decision is certainly correct: even if (which seems unlikely) the judge was wrong on the issue of obviousness, the novelty attack on '281 seems clear-cut and unarguable.'

This was precisely the view of the Court of Appeal, which heard argument from Warner-Lambert's counsel on the question of anticipation, and decided (without

needing to hear from Ranbaxy's counsel) that the judge was correct. In the circumstances, the Court and parties agreed that it was unnecessary to consider the obviousness point in the appeal.

Implications of the decision

The decision regarding the '633 patent will be welcomed by Pfizer and by other research-based pharmaceutical companies. However, other parts of the decision will undoubtedly be seen as helpful by generic manufacturers. First, the decision has implications for patents expressly claiming a single enantiomer of a compound, where the racemate forms part of the prior art. In the previous article, the authors explained why such a patent would be likely to be invalid for lack of inventive step. That is not to say, of course, that an applicant could not obtain such a patent. However, such a patent, if granted, would be likely to be found invalid if subsequently challenged in court.

Given the decision in *Ranbaxy*, the authors submit that it is even more likely that the decision of the EPO Technical Board of Appeal in *Hoechst/Enantiomers* [1990] EPOR 337, in which a patent application claiming a single enantiomer was rejected for lack of inventive step, would be followed by the English courts. Furthermore, it is now possible that the English courts could go further than the EPO in *Hoechst/Enantiomers*. In that case, it was held that a single enantiomer is novel over the racemate. Given that a patent teaching production of a racemate has now been held by the English courts to claim the individual enantiomers as well as the racemate, the authors submit that a challenge to validity on grounds of lack of novelty could also succeed.

Finally, the judgment once again confirms that the English courts carry out a thorough analysis of the prior art, and will not allow patentees to claim a monopoly over what is, in reality, part of the public domain. In particular, it is not permissible for a patentee to extend its protection simply by selecting a subclass of a previously disclosed class of compounds, without setting out clearly what new advantage is claimed for the subclass.

The decision regarding the '633 patent will be welcomed by Pfizer and by other research-based pharmaceutical companies.

The authors understand that both parties are seeking leave to appeal the decision to the House of Lords.

Comparison with other jurisdictions

Ranbaxy is currently contesting equivalent patents in a number of other jurisdictions, including the US and Austria, and is also contesting related process patents in Norway and Finland. This case therefore provides an opportunity to compare the approach of the English courts with those of courts in other countries.

In the US the court at first instance held that Ranbaxy's product infringed the US equivalent of the '633 patent. The US equivalent of the '298 patent was held to be valid. Both decisions were appealed, and the authors understand that the decision from the Court of Appeal for the Federal Circuit is expected in summer 2006.

The Austrian equivalent of the '298 patent has been held invalid, on appeal, in a final decision. The case concerning the equivalent of the '633 patent is ongoing.

Over recent years, a perception has arisen in some quarters that the English courts are in some way 'anti-patentee'. In the authors' view, this is incorrect, as is borne out by the above comparison. The English courts carry out a thorough analysis of a patent's claims, and the relevant prior art, and consequently weak patents may be revoked in circumstances where a less-thorough examination would not have revealed relevant prior art. On the other hand, however, the test laid down by the House of Lords in *Kirin-Amgen* can result in a construction which is favourable to the patentee.

In this particular decision, the English courts have once again deprecated a literal, overly pedantic approach to patent construction, and have stressed that a purposive approach, recognising the way in

which the skilled reader would interpret the wording of the patent and its claims, is mandatory. In doing so, the patent has been construed in a relatively wide and generous manner, and the same decision has been reached as in the US and Austrian courts.

Summary

In summary, the courts in *Ranbaxy* applied a purposive approach to patent construction, adopted a realistic and commercial view of the scope of protection afforded by a patent, and applied the rules governing validity in a strict manner. It is submitted that in so doing, the English courts have demonstrated that they are achieving the combination of 'fair protection for the patentee with a reasonable degree of certainty for third parties' required by the Protocol on the Interpretation of art 69 of the European Patent Convention. ■

Dr Brian Whitehead, solicitor, holds an MA in chemistry (Oxford) and a PhD in biochemistry (Sheffield). Prior to becoming a solicitor, he worked as a research scientist and academic publisher in the Netherlands.

Stuart Jackson, solicitor and director of patent litigation with Addleshaw Goddard, holds BSc (Imperial College) and MSc (Oxford) degrees in chemistry. Prior to becoming a solicitor, he worked in industry as a chemist in R&D for 17 years, and is a Chartered Chemist.

Richard Kempner, partner and national head of intellectual property with Addleshaw Goddard, has acted extensively on cases involving pharmaceutical and chemical patents, including *BASF AG v SmithKline Beecham* and *Mayne Pharma v Teva*.