Neutral Citation Number: [2006] EWCA Civ 876

Case Nos: A3/2005/2592, A3/2005/2598 and A3/2005/2599

IN THE SUPREME COURT OF JUDICATURE
COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE HIGH COURT OF JUSTICE
CHANCERY DIVISION (PATENTS COURT)
The Hon Mr Justice Pumfrey
HC 04 C02167, HC 04 CO2059 and HC 04 CO3986

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 28/06/2006

Before :

LORD JUSTICE CHADWICK
LORD JUSTICE JACOB
and
LORD JUSTICE NEUBERGER

- -

BETWEEN :

Ranbaxy (UK) Limited	**Appellant/ Claimant**
- and -	
Warner-Lambert Company	**Respondent/ Defendant**
-and-	
Arrow Generics Limited	**Intervener**
AND BETWEEN:	
Ranbaxy (UK) Limited	**Respondent/ Claimant**
-and-	
Warner-Lambert Company	**Appellant/ Defendant**
AND BETWEEN:	
Arrow Generics Limited	**Respondent/ Claimant**
-and-	
Warner-Lambert Company	**Appellant/ Defendant**

- -
- -

Andrew Waugh QC and Michael Tappin (instructed by S J Berwin LLP)
for Ranbaxy (UK) Ltd
Andrew Waugh QC and Mark Chacksfield (instructed by Forsyth Simpson)
for Arrow Generics Ltd
Simon Thorley QC and Richard Meade (instructed by Bird and Bird)
for Warner-Lambert Company

Hearing dates : 13th/14th June 2006
- -

Approved Judgment

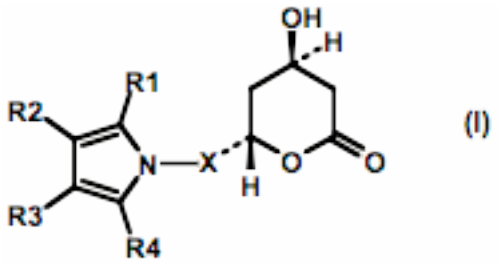
Lord Justice Jacob:

1. This appeal and cross-appeal is from a judgment of Pumfrey J [2005] EWHC 2142 (Pat), [2006] IP & T 336, [2006] FSR 14. He refused Ranbaxy a declaration of non-infringement of Warner-Lambert's EP (UK) 0 247 633 ("633") and held Warner-Lambert's EP (UK) 0 409 281 ("281") invalid for lack of novelty and obviousness. Each side appeals the adverse finding against it, Mr Waugh QC arguing the case for Ranbaxy and Mr Thorley QC that for Warner-Lambert. Another company, Arrow Generics, in the end by consent, joined forces with Ranbaxy. Mr Waugh appeared also for Arrow, advancing no separate case on its behalf.

The '633 Patent and the claimed declaration of non-infringement

2. This turns solely on claim 1. It opens with the words

> "A compound of structural formula I



3. The claim, as is conventional, then goes on to set out possibilities for the various groups. It goes on to include as an alternative a hydroxy acid or pharmaceutically acceptable salts derived from opening out the lactone ring (the ring on the right of the diagram). At [8] the Judge sets the claim out in full but it is not necessary to do so here. What matters for present purposes is that the structure, opened out or not, contains two chiral centres. The Judge explains this in concise, clear and non-controversial terms in [17]-[23] which I reproduce with gratitude:

> "[17] The tetrahedral arrangement of the covalent chemical bonds that a carbon atom may make with four other atoms means that if there are four different units at the ends of the four different bonds those units may be arranged in two different ways. When one says two different ways, it means that no amount of rotating will permit one arrangement to be superimposed on the other. They will be mirror images of each other, and are called enantiomers. This is shown in this diagram:

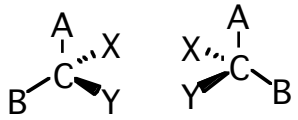


Figure 1. Enantiomers

[18] This is an attempt to show a tetrahedral structure. Conventionally the bonds depicted by single lines are in the plane of the paper: the bonds denoted by a solid wedge (a heavy line may also be used) are out of the paper and the bonds denoted by a dotted wedge (or dotted line) are into the paper. The picture shows two imaginary molecules with an asymmetric carbon atom C. A, B, X and Y denote different atoms or groups positioned at the apexes of the tetrahedron. Because the molecules are handed, they are called chiral, and the asymmetric carbon atom(s) they contain are called chiral centres. A molecule is an enantiomer if it cannot be mapped to its mirror image by rotations and translations alone.

[19] Enantiomers do not differ in any of their physical properties (melting point, boiling point and so on) but one, differing in their effect on plane polarised light. One enantiomer will rotate the plane of polarisation to the left or anticlockwise, and the other will rotate it to the right. A (+) or *d*- is conventionally used to denote the enantiomer which rotates the plane of polarisation to the right, and a (-) or *l*- is conventionally used to denote the enantiomer that rotates the plane of polarisation to the left.

[20] Alternatively, the absolute configuration of the molecule can be worked out according to certain rules. The result of applying the rules is a decision either that the molecule is right-handed (denoted *R*) or left-handed (denoted *S*).

[20] One enantiomer can only be synthesised in preference to the other if the stereochemistry is already present in the starting materials or if enantiomeric reagents are used. Unless the conditions for the reaction are stereospecific the result of the synthesis will inevitably be a 50/50 mixture of the two enantiomers of the chiral molecule. This is called a racemic mixture or racemate. There is no guarantee that the physical properties of the racemate will be the same as the physical properties of the individual enantiomers that go to make it up: for example the melting point may be higher, lower or the same. The racemate has no effect on plane polarised light, the mixture being precisely 50% (+) and 50% (-).

[21] Where there are two asymmetric centres in a molecule, there are unsurprisingly four possible isomers. Looking just at the chiral atoms, both may be mirror images of each other, and the molecules form an enantiomeric pair. If one only is a mirror image of the other, then the molecules are called diastereoisomers. Thus each molecule of the four will have one corresponding enantiomer and two corresponding diastereoisomers. To distinguish the diastereoisomers terminology describing the relative position of significant

groups may be used. If the significant groups are on the same side of a ring, it is called a *cis*- structure, and if on the opposite sides of a ring, it is called a *trans*- structure:

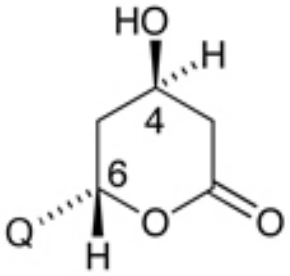
cis trans

Diastereoisomers do not generally have the same properties, and may be separated in reliance on that fact."

4. A particularly helpful diagram setting out the 4 possibilities arising from the two chiral centres, along with the variety of terminologies used was provided as Annex A to Mr Waugh's skeleton argument. I reproduce it here:

Annex A

The Stereoisomeric Consequences of two chiral centres at Positions 4 & 6



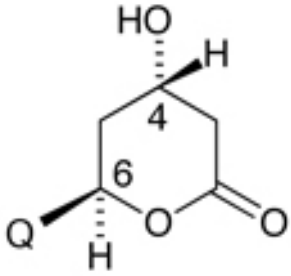
R,R or

4R,6R or

4R-trans or

R (R*,R*)

A



S,S or

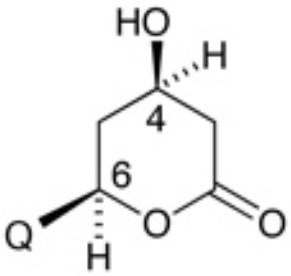
4S,6S or

4S-trans or

S (R*,R*)

B

- A&B are non-superimposible mirror images i.e. a pair of enantiomers
- Both A&B are <u>trans</u> - (i.e. the groups OH and Q at positions 4 and 6 are arranged with one above and one below the plane of the ring)



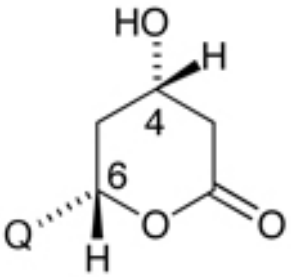
R,S or

4R,6S or

4R-cis or

R(R*,S*)

C



S,R or

4S,6R or

4S-cis or

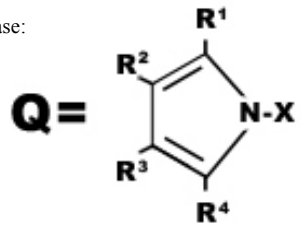
S(R*,S*)

D

- C&D are also <u>a pair of enantiomers</u>
- Both C&D are <u>cis</u> - (i.e. the groups OH and Q at positions 4 and 6 are arranged with <u>both</u> above or below the plane of the ring.)

Mirror plane

In each case:



5. Ranbaxy seek a declaration of non-infringement in respect of a particular compound. It is commonly called atorvastatin calcium. It is the optically pure [R-(R*,R*)]-2-(4-f1uorophenyl)-β,δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)-carbonyl]-lH-pyrrole-1-heptanoic acid calcium salt. The significance of "optically pure" is that the compound is an enantiomer, not a racemate. The Judge used the terminology R-(R*R*) but I will use the shorter, "R,R."

6. Ignoring the stereochemistry, the general structural formula of this compound admittedly falls within claim 1. It is said, however, that its stereochemistry is such as to take the product outside the claim – that the claim only covers the racemic mixture. The short issue is whether the claim is so limited or does it cover the R,R enantiomer too?

7. There was no issue as to how a claim is to be construed. The Judge's summary at [10] was unchallenged:

> "[10] *Kirin Amgen v Hoechst Marion Roussel Limited* [2004] UKHL 46, [2005] RPC 9 (page 169) paragraphs [32] to [35] summarises the modern approach. Extracting short passages may tend to distort the overall meaning of this passage, but from it, and from the approval that it gives to the judgment of Jacob LJ in *Rockwater Ltd v Technip France SA* [2004] EWCA Civ 321, [2004] RPC 6 at [41] (and by inference also to the slightly different statement in *Mayne Pharma v Pharmacia* [2005] EWCA Civ 137 at [5]), I conclude that it is now clear that in deciding what the person skilled in the art would have understood the patentee to be using the language of the claim to mean, the court must approach the problem from the standpoint that the language chosen will be usually of critical importance. An over-meticulous analysis is one that is too willing to draw from a detailed analysis of the grammar, the punctuation and the particular words and phrases used inferences as to meaning that the words might support but which the skilled person would not draw, and it is the antithesis of giving to the words chosen in their context the meaning that the skilled person would give them."

8. The court's first job therefore is to understand enough of the technology to be able to read the patent as it would be read by a man skilled in the art. Here there is now no dispute that such a man would have the knowledge of a medicinal chemist – someone who would be employed by a pharmaceutical company to synthesise new active ingredients. The Judge accepted the evidence of Dr Newton that a medicinal chemist is:

> "a synthetic organic chemist who has got additional training and, in particular, additional training in the biological aspects of pharmaceutical action."

9. Such a person would know about all the matters of stereochemistry I have borrowed from the Judge and set out above. He would also know what the Judge set out at [24]:

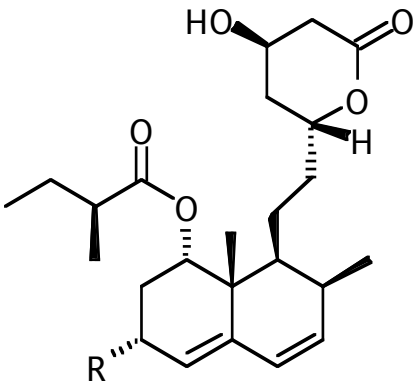
> "[24] Different enantiomers of a chiral molecule react differently with other chiral molecules. This is of particular importance in natural systems since enzymes, which are proteins responsible for all the chemical reactions carried out by the cell, are chiral molecules and are present only as a single enantiomer. I quote Dr Newton's report:
>
> > '15. For many years it has been recognised that the vast majority of drugs exert their activity by binding to a protein receptor to form a drug-receptor complex. Although there are exceptions, this process is usually readily reversible and does not generally involve the formation of covalent bonds. The drug receptor complex is formed by a combination of hydrogen bonds, π-π stacking between aromatic rings, salt bridge formation between carboxylic acids and amines and hydrophobic binding. The particular parts of a drug that cause it to bind to its receptor are together termed the pharmacophore. Since the protein receptors are composed of a complex array of chiral amino acids it follows that the drug's binding site is in a chiral environment (although the drug itself may or may not be chiral).
> >
> > 16. However, in circumstances where the drug substance does have an asymmetric carbon atom or atoms, the binding efficiency to a given receptor and therefore the biological activity of the enantiomers or diastereoisomers will be different. Within a chiral environment the two enantiomers of a racemate are totally different compounds and very often the majority of the biological activity observed for a racemate resides within a single enantiomer. Sometimes both the enantiomers of a racemate are biologically active but act at different receptors and cause different effects.
> >
> > 17. One of the most unfortunate and best known examples of this was the mild sedative and anti-emetic Thalidomide. The drug has an asymmetric centre but was marketed as the racemate. The R-isomer is a non-mutagenic sedative, whilst the S-isomer is mutagenic and caused widespread deformities amongst those children whose mothers took the drug during pregnancy …. Although this is a specific example, the principle was well understood by the skilled person at the 30 May 1986 priority date of the '633 Patent.'
>
> [25] I understood the evidence to be that the skilled person at the priority date would expect that where a drug was a chiral molecule, it was highly likely that only one of the enantiomers and diastereoisomers (if any) would be responsible for its pharmaceutical activity. This did not mean, and does not mean,

> that chiral drugs had to be administered as single enantiomers but there is undoubtedly a modern tendency to prefer single enantiomers where resolution of the racemate is practicable."

10. So if one has a pharmaceutical in the form of a racemate, it is highly likely that only one of the two enantiomers will provide the desired activity or most of it. The other enantiomer will function either as an inert or near inert "filler" or even function partially to inhibit the function of the other enantiomer. It is not suggested that the presence of the "inert" enantiomer is at all likely to enhance the function of the "active" enantiomer.

11. The skilled person would also know something about prior art statins. The Judge summarised this uncontroversially:

> "[26] The other aspect of the common general knowledge which it is necessary to consider is the common general knowledge in respect of statins generally. By 1986, statins were a well-known class of compounds recognised as having a potential application for cholesterol-lowering drugs. The first statins, mevinolin and compactin, were natural products that existed as single enantiomers. Much work had been done on these compounds, and it was recognised that they had a 4(R)-*trans*- structure:



> In compactin, R= H, and in mevinolin R=CH_3.
>
> It may be seen that the lactone ring in the top right of the structure is the same as the lactone ring of formula I of the patent. What is different is the substituent at the 6 position on that ring.
>
> [27] The document called Stokker ('3-Hydroxy-3-methylglutaryl coenzyme A Reductase Inhibitors' J Med Chem 1985 28, 347-358 also seems to have been accepted to be a document the skilled person would undoubtedly become aware of in doing any statin work, if not common general knowledge in the strict *Beloit v Valmet* sense, at the priority date. It reports a substantial statin study, and both Prof Clive and Dr Newton

> said that it disclosed that it was likely that all the activity lay in the 4(R)-*trans*- isomer.
>
> [28] It was also known that the active form of the molecule was the open-chain hydroxy acid formed by hydrolysing the lactone ring. This acid can readily form salts, for example the sodium salt."

12. The Judge also stated common general knowledge at [37]:

> "i)The skilled person knew that compactin and mevinolin were potent anti-cholesterolaemics, and were single (R, R) enantiomers;
>
> ii) He knew from Stokker that it was likely that all active compounds of this description would be single *trans*-enantiomers, the (R,R) enantiomers, the (S,S) enantiomers being likely to have no activity;
>
> iii) He knew from his common general knowledge that a racemic mixture can be resolved into its component enantiomers."

13. Equipped with the common general knowledge one can turn to the patent. For present purposes only a few passages matter. Adjusting for an appalling blunder by way of misprint, it begins:

> "The present invention is related to compounds and pharmaceutical compositions useful as hypocholesterolemic and hypolipidemic agents. More particularly, this invention concerns certain [classes of compound] which are potent inhibitors of the enzyme [name set out] …"

Some prior art is then acknowledged. It includes mevinolin and compactin. The final acknowledgement (of EP A 179559) is about a structure similar to that of Formula I but with different substituents in the 3 and 4 positions on the pyrrole (left hand) ring. The patent then says:

> "the specification, however, does not mention the 3- or 4-carboxamido-substitution, which makes the compounds surprisingly more active."

This reflected the title of the patent itself: "Trans-6-[2-(3- or 4-Carboxamido-substituted pyrrol-1-yl)-alkyl]-4-hydroxypyran-2-one inhibitors of cholesterol synthesis". The heart of the teaching, submitted Mr Thorley, is that this particular substitution produces a surprising increase in activity. The emphasis is on what has been put onto the pyrrole ring, not the lactone ring (opened out or not). The centre of the teaching is about that, not about stereochemistry at all.

14. I accept that submission. It is borne out by the fact that the patent says very little about stereochemistry at all. All there is is this:

> 'The compounds of structural formula I above possess two asymmetric carbon centers, one at the 4-hydroxy position of the pyran-2-one ring, and the other at the 6-position of the pyran-2-one ring where the alkylpyrrole group is attached. This asymmetry gives rise to four possible isomers, two of which are the R-*cis*- and S-*cis*-isomers and the other two of which are the R-*trans*- and S-*trans*-isomers. This invention contemplates only the *trans*- form of the compounds of formula I above.' (p.$4_{8\text{-}12}$)

15. This short passage is, to my mind, a clear indication that the patentee is concerned with the *trans*-form of the compounds of formula I. There are two of these, R,R and S,S.

16. The patent then goes into the detail of how the compounds are to be made. It is sufficient to note that all that is explicitly described is production of the racemate.

17. The Judge at [38] – [41] reasoned and held that claim 1 covers the racemate and the individual enantiomers. The heart of his reasoning is [41]:

> "[41] In the '633 patent, it is absolutely clear from context throughout that formula (I) is being used to denote a racemate. In my judgment, every time the skilled person sees formula I or formula X he will see it with eyes that tell him that in that racemate, there is a single enantiomer that is the effective compound, and that he can resolve the racemate using conventional techniques to extract that enantiomer. When one comes to claim 1, which echoes the purpose of the invention with its conventional reference to pharmaceutically acceptable salts, he will, in my judgment, continue to see the formulae in this light."

18. Mr Waugh's attack on this reasoning, although expounded at length, can be stated shortly:

    i) The only method of production of the compounds described in the patent produces the racemate;

    ii) The perception of the skilled man will be that the S,S-enantiomers will have no effect;

    iii) So he will think the patentee cannot have intended to claim the S,S-enantiomers – especially so since the patent opens with the promise that the invention is related to "potent" compounds;

    iv) This is reinforced by the fact that if the patent indeed covered the S,S-enantiomers it would be invalid on the grounds of insufficiency ("invention not disclosed clearly enough and completely enough for it to be performed", s.72(1)(c) of the Patents Act 1977). Mr Waugh particularly relied on *American Home Products v Novartis* [2001] RPC 159 and *Pharmacia v Merck* [2001] EWCA Civ 1610; [2002] RPC 775;

v) Since it is common ground that the skilled man would have known how to resolve the racemate, the patentee could readily have claimed the R,R-enantiomer explicitly. That he failed to do so would be taken by the skilled reader as a deliberate decision not to claim it;

vi) There would be good reason for limiting the monopoly claimed to the racemate. In particular the patentee had done no work with the enantiomer and had no data on it. Moreover at the date of the patent many chiral pharmaceuticals were in racemic form. So a monopoly over the racemate only would be of value.

19. I do not accept this. Overshadowing everything is the fact that the skilled reader would know that the R,R-enantiomer was the form which had all or by far the preponderance of the pharmaceutical activity. He would expect the patentee to know that too. And he would know that the patent claim was drafted by someone who knew what its function was – to "demarcate the invention" (*per* Lord Hoffmann in *Kirin* at p. 185). There simply is no rational basis for supposing that the patentee would want to exclude the pure enantiomer which he would have known was the substance which really mattered.

20. Mr Waugh's suggestions as to why the patentee would want to limit the monopoly to the racemate simply do not stand up – they are merely reasons why he would want to cover the racemate too. True it is that "a patent may, for one reason or another, claim less than it teaches or enables" (*per* Lord Hoffmann at p.186) but that is not a reason for interpreting the claim in the context of the patent in a way that no rational patentee would have intended.

21. Lord Diplock said in the *Antaios* case [1985] AC 191, 201:

> "I take this opportunity of re-stating that if detailed and semantic analysis of words in a commercial contract is going to lead to a conclusion that flouts business commonsense, it must be made to yield to business commonsense"

Lord Hoffmann made it clear in *Kirin* at [31] that this applies equally to the construction of patent claims. It applies here.

22. Moreover the actual drawing of formula I and of X shows what is, strictly speaking, just the R,R enantiomer (compare drawing A on Annex A with Formula I). It was common ground that in practice chemists are not precise: that a figure showing a particular structure may mean, in context, a racemate. The Judge held that, in the context of the patent, Formula I would have been understood to show the racemate. However, I can think of no rational reason why it should mean *only* the racemate in the context of this patent. It is a patent whose big idea is not about stereochemistry but about a novel substitution. The only reference to stereochemistry excludes the "cis-form" of the compounds (which would be both cis-enantiomers) but not the trans- form (which would be both trans- enantiomers). And above all the skilled reader would know that the form giving most if not all activity was the R,R form.

23. Mr Waugh sought to persuade us that the evidence established an unvarying convention such that, whatever the context, a figure showing a particular enantiomer

denoted only that enantiomer or only the racemate. Putting it another way, there is a convention that, whatever the context, such a figure could not mean both the racemate and/or either enantiomer. If such a convention had been proved that would of course bear directly on the construction of the claim – for although in the end the question of construction is for the court, the court will have to go by any proved term of art or proved system of nomenclature. This is because a skilled man would read the document using such a convention.

24. The argument fails. The existence or otherwise of such a convention is one of fact, not law. The Judge made no such finding of fact. Indeed by his ultimate conclusion he necessarily implicitly rejected such a finding. Mr Waugh therefore had to argue that the Judge had made a wrong finding of fact – never an easy task in the Court of Appeal. He relied on certain passages in Professor Clive's evidence, e.g. §83. He could point to no textbook setting out such a convention – which is the normal way of proving a system of nomenclature. Moreover Mr Thorley drew to our attention a number of passages in the cross-examination of Professor Clive and Dr Newton, which show that what a formula means (racemate, enantiomer or either) depends entirely on context. In some contexts it will mean one or the other but not both but that is all. The Judge was not shown to be wrong.

25. As to Mr Waugh's point about the S,S enantiomer, even if he were right in saying that the skilled man would perceive it as having no activity whatsoever, I do not think the skilled man would read the claim as excluding the key active enantiomer. He would be much more likely to say to himself, "Well I see the claim covers the inactive form too". He might add: "I do not know why – I know how to make it, how to resolve it out of the racemate, but so what?" He would not, I think, say to himself: "The patent promises that the carboxamido substitution will give surprisingly more activity, so the formula cannot include the inactive S,S and it follows it cannot also include the key active R,R compound." That would be just foolish. Such reasoning reeks of an overmeticulous rather than purposive approach. It is one that flouts technical and business commonsense. It may have a kind of crazy logic but it will not do.

26. Nor do I think that *American Home Products* or *Pharmacia* help Mr Waugh. We are, after all, concerned with the construction, and construction only, of this patent. Those were cases about validity and construction of different patents. In *American Home Products* the issue was whether the word "rapamycin" in the context of the patent covered not only the compound as such but any derivative of rapamycin which worked. The skilled man would, without experiment, have no idea whether any particular derivative worked. If the claim was as contended for by the patentees it would be "a starting point for a research programme" (*per* Aldous LJ at p.178). That was a reason for not giving it the wide construction contended for. There is no analogy with this case.

27. *Pharmacia* was concerned with a similar problem. The claim covered a wide range of compounds said to be Cox II inhibitors. In fact some were, others not – and you could only find out whether one was or not by experiment. The patent was held invalid for insufficiency. In this case there is simply no attack on sufficiency – all that is relied upon is an alleged perception of the skilled man that the S,S enantiomer is totally inactive as a reason for his thinking that the pure active R,R enantiomer is excluded. Bizarre logic indeed.

28. So even if Mr Waugh's assumption that the skilled man would perceive the S,S enantiomer to have no activity whatsoever is right, I see no reason to read the claim as limited to the racemates. Of course if the assumption were wrong the whole argument would fail anyway. Mr Thorley submitted that was so – that it was never proved that the skilled man would have the perception of no activity Mr Waugh said the Judge had so found, relying on several passages in the judgment:

> [Talking about Stokker's discussion of the prior art compounds] [27] "… both Prof Clive and Dr Newton said that it disclosed that it was likely that all the activity lay in the 4(R)-*trans*- isomer"
>
> "He knew from Stokker that it was likely that all active compounds of this description would be single *trans*- enantiomers, the (R,R) enantiomers, the (S,S) enantiomers being likely to have no activity" [37]
>
> "the near certainty that only one enantiomer composing the racemate will matter" [38]

29. I think Mr Thorley is right. The Judge did not hold that the skilled man would be sure the S,S enantiomer had no biological activity at all. That was not so for chiral compounds generally (see e.g. §16 of Dr Newton, quoted by the Judge). The fact that there was no activity shown for the S,S compounds of the prior art statins made it very likely that there would also be no measurable activity for the S,S compounds of the claim. But no more. It was never actually proved that they actually have no activity or that the skilled man would be certain that was so. So this is another reason for rejecting Mr Waugh's argument – an argument which in any event was advanced rather late, not having been raised until after the cross-examination of Dr Newton.

30. Finally on construction I should mention the claim 3 point. This claim relates to a specific compound "having the name trans-(±) ….". The symbol ± means a racemate. Each side prays claim 3 in aid as throwing light on claim 1. The Judge thought the point was neutral. So do I. One the one hand one can say that the patentee uses the symbol when he wants to denote only the racemate so claim 1 must be wider. On the other because claim 1 is to a vast number of compounds, it could be that, even if all of the claim 1 class were intended to be racemates, that when being much more specific about a single compound, the patentee was just being somewhat more precise.

31. I therefore think the Judge was right to refuse the declaration of non-infringement. It is agreed that the attack on the SPC falls with that decision.

The validity of Patent EP (UK) 0409 281

32. The judge held this patent anticipated by a prior earlier co-pending application WO 89/07598 and obvious over a prior published international application, EP 0247 633A. We heard Mr Thorley first on the question of anticipation. We did not need to hear Mr Waugh by way of response because we formed the view, despite Mr Thorley's admirably concise argument, that the Judge was right. In those circumstances we asked Mr Thorley whether there was any point in our hearing the obviousness appeal. He said there was none. The only way in which obviousness could become a live

issue would be if our decision on anticipation were both heard and reversed by the House of Lords. Given the House's recent decision on patent novelty in *Synthon's Patent* [2005] UKHL 59, [2006] IP & T 61, it was most unlikely that either we or it would give leave to appeal. So we decided not to hear the obviousness appeal.

33. On anticipation the basic law was not in controversy. The combined effect of s.2(3) and s.3 of the Patents Act 1977 (corresponding to Arts. 54(2) and (3) and Art. 56 of the European Patent Convention) is that an unpublished earlier co-pending application is available only for an attack of want of novelty.

34. Mr Thorley took to two passages in Lord Hoffmann's speech in *Synthon*. After citing two well-known passages from English cases, *Hill v Evans* (1862) 31 LJ(NS) 457 at 463 and *General Tire v Firestone* [1972] RPC 457 at 485-486) Lord Hoffmann said:

> "[22] If I may summarise the effect of these two well-known statements, the matter relied upon as prior art must disclose subject-matter which, if performed, would necessarily result in an infringement of the patent…… It follows that, whether or not it would be apparent to anyone at the time, whenever subject-matter described in the prior disclosure is capable of being performed and is such that, if performed, it must result in the patent being infringed, the disclosure condition is satisfied. The flag has been planted, even though the author or maker of the prior art was not aware that he was doing so."

Although the rule is found in those old cases, it remains the rule under the European Patent Convention and the UK-see s.2(1) of the 1977 Act. You cannot monopolise that which forms part of the state of the art.

35. The second citation included approval of what was said by an EPO Board of Appeal:

> "[23] … But the prior disclosure must be construed as it would have been understood by the skilled person at the date of the disclosure and not in the light of the subsequent patent. As the Technical Board of Appeal said in *T/396/89 UNION CARBIDE/high tear strength polymers* [1992] EPOR 312 at para 4.4:
>
> > 'It may be easy, given a knowledge of a later invention, to select from the general teachings of a prior art document certain conditions, and apply them to an example in that document, so as to produce an end result having all the features of the later claim. However, success in so doing does not prove that the result was *inevitable*. All that it demonstrates is that, given knowledge of the later invention, the earlier teaching is capable of being adapted to give the same result. Such an adaptation cannot be used to attack the novelty of a later patent.'"

36. That being the law, I can turn to this case. Claim 1 of '281 is to a single compound, the hemicalcium salt of [R-(R*,R*)]-2-(4-f1uorophenyl)-β,δ-dihydroxy-5-(1-

methylethyl)-3-phenyl-4-[(phenylamino)-carbonyl]-lH-pyrrole-1-heptanoic acid, known as atorvastatin calcium. It is the compound from which the commercial pharmaceuticals are made and which has the SPC. It is an enantiomer, the R,R form.

37. Mr Thorley took us to p.40 which shows a reaction scheme which, because it is non-stereospecific, will produce a racemate. Compound XII is the acid of the later claimed salt, albeit in racemic form only.

38. Then the citation says at p.43 that the acid can form a salt, mentioning specifically calcium:

> "In the ring-opened dihydroxy acid form, compounds of the present invention react to form salts with pharmaceutically acceptable metal and amine cations formed from organic and inorganic bases. The term "pharmaceutically acceptable metal salt" contemplates salts formed with the sodium, potassium, calcium, magnesium, aluminum, iron and zinc ions."

39. So there is clear disclosure of the salts of the acid. Mr Thorley felt constrained to accept that there was a prior disclosure at this point of the salts of the racemates, including the calcium salt. What he submitted was not specifically disclosed up to this point was the salt of the pure enantiomer. And that is true. But on the next page '598 points out that there are two asymmetric carbon centres and goes on to say:

> "The preferred isomer in this invention is the 4R,6R-isomer of the compounds of Formulas I, Ia and XII above"

40. To my mind this, in context, clearly teaches by way of explicit disclosure that one of the things you can make is the single enantiomer of the acid and it is that acid which can be used to make the calcium salt. In truth that way of carrying out the teaching of the earlier patent would necessarily infringe the later claim. So that claim is invalid as lacking novelty. I reject Mr Thorley's submission that one is here straying into the impermissible territory of obviousness. Alighting on atorvastatin calcium is merely picking one of the class of compounds disclosed by '598. If the claim were valid it would cover one of the alternatives explicitly taught by the citation. This is not a case of any adaptation of the prior art.

41. The Judge put it this way:

> "[49] It follows that the material claimed in claim 1 is an expressly specified salt (calcium) of the preferred isomer of one of the three materials explicitly specified. If one is in any doubt, it is easy to compare the final structural formula on page 12 of '281 against formula XII on page 40 of '598. They are identical, save that in '281 the calcium salt, and in '598 the acid, are shown. In fact, the synthetic route described in '598 actually produces a racemate. But this time, the precise enantiomer (4R,6R) is specified. This notation means the same thing as the [R-(R*,R*]… used in respect of the acid in claim 1 of '281. The evidence (which I have already discussed) was

> that resolution to obtain the enantiomers was common general knowledge. It is no answer to an allegation of anticipation that the specification gives clear and unmistakable directions to use the common general knowledge to produce a specific material."

That seems to me to be both elegant and clearly right.

42. In the result I would dismiss the appeal and cross-appeal.

Lord Justice Neuberger:

43. I gratefully adopt the succinct recital of the facts as set out in the judgment of Jacob LJ. I would like to add a few words of my own on the point raised on the appeal, which is effectively whether claim 1 in '633 extends only to the racemic mixture, as Mr Waugh contended, or whether, as the judge held, and Mr Thorley argued, it also extends to the two enantiomers.

44. Mr Waugh's main argument was based on the fact that the Judge concluded (a) that the formula shown in claim 1 (as set out in [2] of Jacob LJ's judgment) would have been understood by the reader to be the racemate (see [41] of the judgment), and (b) that the racemate was the racemic mixture which would have been regarded as a different substance from either of the two enantiomers of which it was composed (see [21] of the judgment). In my view, both components of that argument are flawed. I shall deal first with component (b), and then with component (a).

45. The fact that the racemate manifests, or may manifest, different physical properties from the pure enantiomers does not alter the fact that it is a 50/50 mixture of the two enantiomers. In particular, that proposition applies to a racemate in relation to its pharmaceutical aspect, which is the centrally important aspect for present purposes. As the Judge explained in [24], where a racemate is administered as a drug, one enantiomer is likely to have all, or the great majority, of the biological activity, and that activity will be either unaffected or reduced by the presence of the other enantiomer. The fact that the racemate in the present case has the claimed pharmaceutical effect shows that it is no exception. This demonstrates that the sole or mainly effective enantiomer maintains its character and (at least to a substantial extent) its effectiveness, notwithstanding that it is administered as part of a racemic mixture.

46. Accordingly, it appears to me that it is wrong to conclude that a racemate, and in particular the racemate in this case, cannot be regarded as a mixture of the two enantiomers. That does not involve holding that a racemate cannot also be regarded as a racemic mixture, i.e. a different substance from the two enantiomers. Indeed, so to hold would be to fly in the face of the evidence. However, the two propositions are not mutually inconsistent. "A+B" can be regarded both as a single entity, namely (A+B), and as a mixture of two entities, namely A and B.

47. Whether it is possible to regard "A+B" as a mixture of A and B as well as (A+B), as opposed to regarding it as only (A+B), must depend on the facts and

on the context. Thus, in most contexts at any rate, one would not regard common salt as a mixture of sodium and chlorine: it would solely be regarded as sodium chloride. However, it would be much easier to argue in many contexts that, in an aqueous solution, it could be regarded as a mixture of salt and water as well as being regarded as saline.

48. I turn to Mr Waugh's point that the Judge's conclusion that the reader of the patent would have understood the formula shown in claim 1 to be a racemate means that the claim only extends to the racemic mixture, and not to either of its constituent enantiomers individually. As already mentioned, it appears to me that it must be a question of construction, to be determined by reference to the words of the patent and business common sense, whether the reference to the racemate, as shown by the formula in claim 1 is a reference to the racemic mixture alone or to that mixture and to its constituent enantiomers. The proper approach to construction in this connection is not in doubt, and was set out in [10] of the judgment of Pumfrey J.

49. Subject to the point considered in the next paragraph but one, it seems to me clear that the formula in claim 1 must be a reference to the enantiomers as well as the racemic mixture. As the notional addressee of the patent, the relevantly skilled person, would appreciate, it would have been absurd for the patentee to have limited his claim to the racemic mixture. Given that one of its two constituent enantiomers would have been, at best less effective than, or, at worst, ineffective and detrimental to the effectiveness of, the other enantiomer, it would make no practical sense to construe the formula as extending only to the racemic mixture and not to the latter enantiomer.

50. In this connection, I should refer to the Judge's finding that the relevantly skilled person would know how to resolve the racemate (i.e. how to isolate the (more) effective enantiomer) and he would know that this would be generally appreciated by those skilled in the art. That may well be of crucial significance. First, in terms of teaching, the patent is thereby not rendered insufficient if it claims the enantiomers, notwithstanding any express teaching as to how to resolve the racemic mixture. Secondly, the finding underlines the commercial unreality, actual and as perceived by the skilled person, of the contention that the claim does not extend to the enantiomers.

51. Mr Waugh submitted that, if claim 1 extends to the (more) effective enantiomer, it must also extend to the other enantiomer, and, as that other enantiomer is ineffective, the claim would be insufficient. I would reject that argument for two separate reasons. First, it was not established that either of the enantiomers was, or would have been assumed by the skilled person to be, ineffective, and the Judge did not so find. Secondly, even if that had been established, it appears to me that the skilled man would have interpreted the claim as extending only to the effective enantiomer (for the reason given by Jacob LJ in [25] above). In addition it should be added that, even if the claim extends to the (assumed for this argument) ineffective enantiomer, I regard it as an open question whether that would thereby render the claim, extending as it still would to the racemate and the effective enantiomer, invalid. The claim would, on this hypothesis, admittedly extend to an ineffective substance, but it would still be a new compound.

52. For these reasons, which are much the same as the reasons expressed by Jacob LJ (with which I agree), I would dismiss the appeal. For the reasons given by Jacob LJ, I would also dismiss the cross-appeal.

Lord Justice Chadwick:

53. For the reasons set out in the judgments of the other members of the Court, I agree with the order proposed by Lord Justice Jacob.