Case No: A3/2012/1105, A3/2012/1107 & A3/2012/1108

Neutral Citation Number: [2013] EWCA Civ 454

IN THE COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT
THE HON MR JUSTICE ARNOLD
Claim Nos. HC11 C01095, HC11 C00553 & HC10 C04779

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 30/04/2013

Before :
THE CHANCELLOR OF THE HIGH COURT
LORD JUSTICE MUMMERY
and
LORD JUSTICE McFARLANE

- -

Between :

ASTRAZENECA AB	**Appellant**
- and -	
HEXAL AG & ORS	**Respondent**

- -

(Transcript of the Handed Down Judgment of
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Official Shorthand Writers to the Court)

- -

MR SIMON THORLEY QC, MR PIERS ACLAND QC and MR MARK CHACKSFIELD (instructed by Bristows LLP) for the Appellant

MR DANIEL ALEXANDER QC and MR ADRIAN SPECK QC (instructed by Pinsent Masons LLP on behalf of Teva and Taylor Wessing LLP on behalf of the other respondents) for the Respondents

Hearing dates: 17th and 18th October 2012

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Judgment

Lord Justice Mummery:

Introductory summary

1. This case is about the validity of a European Patent (UK) No. 0, 907, 364 (the Patent). It is for sustained release formulations of an anti-psychotic drug called quetiapine.

2. According to the 6 claimant companies the Patent is invalid. They say that what is claimed in the Patent to be an inventive step would, at the priority date (May 1996), be obvious to the notional addressee skilled in the prior art.

3. The claimants crisply summarise the essence of their case on obviousness in this way. They point to the Patent as itself recognising the general desirability of a sustained release form of a pharmaceutical. The Patent specifically draws attention to the well-known advantages of such formulations: they are able to provide a stable and desired blood plasma level of the active ingredient, without the need for frequent administration. That recognition accords with the common general knowledge that sustained release formulations provide significant advantages: more stable dosing over a period and the possibility of less frequent administration. The use of the gelling agent involved was not inventive. The materials before the trial judge showed that there was clear motivation to make a more-convenient-to-take, once-a-day formulation. There was no technical reason to suppose that it would have been difficult to make such a formulation: indeed, it would have been straightforward. None of the points, which were put up by the defendant patentee to suggest that a skilled person (in this case a skilled team) would have been put off, would, in fact, have deterred the skilled person from actual trial.

4. The claimants cited in support the observations of Jacob LJ in what they say is a very similar case to this on the facts and the law: *Actavis v. Novartis* [2010] EWCA Civ 82; [2010] FSR 18 at [61]-[64]. In that case this court rejected an appeal against the finding of obviousness of a sustained release formulation of a drug fluvastatin, which involved no technical difficulty and produced improved patient compliance. Mr Simon Thorley QC appearing for the patentee, AstraZeneca AB, cautioned the court against reliance on *Actavis v. Novartis.* He submitted that that case turned on its own facts. In at least four respects those facts were to be contrasted with the facts in this case. There were significant differences between the *Novartis* patent and the Patent in this case. Mr Thorley QC cited a contrary recent authority on the question of obviousness in relation to sustained release formulations: *Ratiopharm GmbH v. Napp Pharmaceutical Holdings Ltd* [2008] EWHC 3070 (Pat); [2009] RPC 11; and [2009] EWCA Civ 252; [2009] RPC 18. In that case the claim for revocation of the patent in suit failed, whereas it succeeded in *Novartis.*

5. The Patent is valid according to AstraZeneca, which markets quetiapine under the name Seroquel XL in sustained release form prescribed for the treatment of schizophrenia, bipolar disorder and major depressive disorder. The essence of its case against obviousness is that, at the priority date, no dosage form of quetiapine was approved or on the market. It was inventive to think of what the Patent provides in the light of the problems alleged to exist. At the priority date there was no perceived advantage or motivation to formulate quetiapine as a sustained release dosage form. The skilled addressee would have been put off from doing so.

6. Mr Thorley QC emphasised the importance of noting at the very outset that the claimants did not advance any case at trial that there was any motivation or desire for a sustained release formulation of quetiapine *per se*. The claimants' case was that there was a motivation to provide a once-a-day formulation of quetiapine. That would in turn lead to a consideration of sustained release formulations. Absent the alleged desire for once-daily dosing, it was not suggested that the skilled addressee would have had any reason to consider a sustained release formulation of quetiapine.

7. According to the excellent judgment of Arnold J, handed down after a 5 day trial of 3 actions with 4 expert witnesses, the claimants are right about obviousness. There was no inventive step. He revoked the Patent by his order dated 24 April 2012 on the ground that, in the light of the prior art and the common general knowledge, the relevant claim was obvious. He found that the skilled person would regard a once-a-day formulation as desirable; that, in order to achieve that result, a sustained release formulation and a higher dose of an immediate release formulation would both be obvious possibilities; that the skilled person would not expect, from his common general knowledge or from a literature search, that quetiapine was likely to saturate on first pass metabolism and would not, therefore, be deterred from developing a sustained release formulation, nor would its expectation of success be adversely affected; and the skilled person could achieve success without difficulty.

8. According to AstraZeneca's Notice of Appeal the judge was wrong about practically everything that he decided in his judgment, save, it seems, for his order granting AstraZeneca permission to appeal and a stay of the order for revocation pending the outcome of the appeal.

9. The grounds of appeal relied on by AstraZeneca have been revised, as explained below, but are still quite lengthy. They are that the judge erred in principle in not considering the allegation of obviousness on the basis advanced by the claimants in their evidence regarding the development of a new formulation of quetiapine starting from Gefvert (see below) and the clinician's reasons for recommending once-daily dosing in preference to twice-daily dosing, and the requirement for those recommendations to be based on clinical considerations. The judge did not consider whether the clinician's common general knowledge provided any, or any sufficient, motivation to overcome the teaching in Gefvert that once-daily dosing of quetiapine was unlikely to be efficacious. In any event, the judge erred in his analysis of the situation. He should have considered matters in the round, but instead considered matters on an impermissible stepwise basis without ultimately considering the cumulative effect of all the relevant factors.

10. In particular, the judge erred in identifying the roles of the different members of the notional skilled team, which he identified as the skilled addressee, at different stages in the notional project, such as who should be regarded as the leader, the clinician or the formulator; in concluding that there was any motivation for the skilled addressee clinician to propose the development of a once-a-day formulation; in adopting an impermissible "step wise" approach to the question of inventive step and to the identified factors that would have led the skilled addressee to have concerns over the development and effectiveness of a once-a-day sustained release formulation of quetiapine and would put a skilled person off from actual trial in detail; and in adopting the wrong approach in law to the issue of obviousness, contrary to what is laid down in the authorities.

11. A central criticism of the judgment is that it failed to address AstraZeneca's case *as a whole* on the key question. That question was the skilled addressee's expectation of success in being able to make an improved formulation of quetiapine using sustained release technology in the combined light of the totality of the points made by AstraZeneca, such as reduced efficiency, side effects, lack of information on key matters and other concerns.

12. Had the judge not erred, he would, AstraZeneca contends, have reached the same conclusion as reached by the District Court of the Hague (see below) and held Claim 1 to be valid for the same reasons. There was no, or insufficient, motive for the clinician to recommend once-daily dosing of quetiapine in the light of Gefvert and his common general knowledge, coupled with the fact that the prospect of making a sustained release formulation with an adequate efficacy and side-effect profile was at best uncertain.

13. The response of the claimants to those criticisms of the judgment by AstraZeneca is that there is nothing in any of them that could lead this court to overturn the judgment of Arnold J: this appeal is a re-run of the arguments on evidential points and factual matters rejected by Arnold J. He was the judge of fact. This court is not. The facts were decided by the Judge against AstraZeneca in accordance with the evidence and he reached his conclusions by applying the correct legal principles relevant to the statutory test of obviousness.

14. According to the judgments of patent courts in some other jurisdictions, there is a considerable range of informed legal opinion about the alleged obviousness of the claimed inventive step in equivalent patents. Ongoing litigation in the courts of other countries about the validity of patents equivalent to the Patent featured in the decision below was a factor affecting the judge's decision to grant permission to appeal. The District Court of the Hague gave judgment in March 2012 rejecting the contention of one of the claimants in these proceedings (Sandoz) that the equivalent patent was invalid for obviousness. The Spanish Courts have also upheld the validity of the equivalent patent. The German Courts granted relief in infringement proceedings on the basis that the equivalent patent was valid.

15. Since the hearing of the appeal the parties have notified the court of further developments in other jurisdictions. On 13 November 2012 the Federal Patent Court declared the German equivalent patent invalid for obviousness. On 14 February 2013 the United States Court of Appeals for the Federal Circuit unanimously upheld the lower court's ruling in *AstraZeneca v. Anchen Pharmaceuticals & Ors* that the formulation patent protecting SEROQUEL XR (quetiapine fumarate) extended release tablets in the US is valid and infringed. On 7 March 2013 the Ontario Federal Court held in *AstraZeneca Canada Inc & Anor v. Teva Canada Limited & Anor* that the equivalent patent was invalid on applying a test of obviousness similar to that applied in the English Courts.

16. The widely disputed validity of equivalents to the Patent does at least go some way towards validating an ancient aphorism *Quot Homines Tot Sententiae*. The different *Homines* obviously all think that their *Sententiae* are right. The truth is that they may well be, when they are considered on the basis of the actual evidence and the particular legal submissions before them in the different proceedings in the various courts. Judicial decisions on obviousness turn on the evidence adduced by the parties,

on the arguments advanced on their behalf and on the adjudicating body's understanding of all the materials before it.

17. Fortunately, we do not have to decide whether the judgments of other courts in different jurisdictions are right or wrong. In this case in this court appellate judging is a more modest enterprise: all that we have jurisdiction to decide under Part 52 CPR is the more manageable question whether the order made by Arnold J was, on the evidence and arguments before him, wrong. If it was not, we have no jurisdiction under Part 52 to set aside his order and we would have to dismiss AstraZeneca's appeal.

The issues

18. Originally two claims in the Patent were in issue.

19. The first was claim 1. It was for a sustained release formulation of an anti-psychotic drug known as quetiapine or seroquel. It was formulated by use of a gelling agent. The judge held that a sustained release formulation would, at the priority date, be, to the notional person skilled in the prior art, an obvious way of achieving the desirable objective of daily administration of the drug.

20. The second was claim 15. It was for formulations also containing a material known as sodium citrate as a pH modifier.

21. Only claim 1 is live in this appeal. AstraZeneca has made it clear that it does not agree that the judge was correct in holding that claim 15 was invalid and that it does not make any concessions. The court was informed during the hearing of the appeal that AstraZeneca no longer asks the court to consider claim 15, or certain other grounds originally raised in the Appeal Notice, notably the point that the judge wrongly concluded that the skilled formulator would have approached the task of formulating quetiapine with a general expectation that its first pass metabolism would not be saturated by the clinical dose.

22. AstraZeneca submitted a marked up version of its Grounds of Appeal indicating the grounds that this court needs to consider. It emphasised that it does not concede or accept that Arnold J was correct or entitled to find as he did in relation to the other grounds.

23. Mr Simon Thorley QC for AstraZeneca and Mr Daniel Alexander QC for the claimants argued the remaining grounds with commendable conciseness and lucidity.

General background

24. Arnold J set out the background in his judgment [2012] EWHC 655 (Pat).

25. The detail in a first instance judgment of such obvious quality does not need to be repeated to the same extent in the decision on appeal. The only issue is whether the order under appeal was wrong. This judgment can keep to those points that are essential for an understanding of AstraZeneca's grounds of appeal, its arguments as to why Arnold J's decision was wrong and the claimants' reasons for upholding that decision.

26. Claim 1 in paragraph [0001] states that the invention relates to a sustained release pharmaceutical composition comprising quetiapine or a pharmaceutically acceptable salt thereof. Paragraph [0002] of the specification states:

> "It is desirable in the treatment of a number of diseases, both therapeutically and prophylactically, to provide the active pharmaceutical ingredient in a sustained release form. Desirably the sustained release provides a generally uniform and constant rate of release over an extended period of time which achieves a stable and desired blood (plasma) level of active ingredient without the need for frequent administration of the medicament."

27. The judge reviewed the evidence on formulation common general knowledge by reference to routes of administration (oral); immediate release formulations; and the main advantages and limitations of sustained release formulations. He also reviewed the situation on compliance, both from the clinician's perspective and from the formulator's perspective, on prescribing practice and on convenience.

28. His overall conclusion, based on the evidence as a whole, was that the skilled team would regard once-a-day formulation of quetiapine as preferable. That was on the grounds that it might lead to better patient compliance and it was more convenient to both patients and carers. The skilled team would also have been well aware that one of the advantages of sustained release formulations was that they enabled less frequent administration, in particular, once a day rather than twice a day.

Obviousness: law

29. The correct approach in law (a) to the issue of obviousness and (b) to an appeal from the decision of the trial judge on such an issue is so well settled that it would be pointless to review and impertinent to revise what other, more expert judges, have repeatedly said in the cases cited in argument, such as *Biogen v. Medeva* [1997] RPC 1 at 34*; Conor Medsystems Inc v. Angiotech Pharmaceuticals Inc* [2007] EWCA Civ 5; [2007] RPC 20*;* [2008] RPC 28; *Generics (UK) Ltd v. H Lundbeck A/S* [2007] EWHC 1040 (Pat); [2007] RPC 32 at [72].

30. The ultimate question of fact for Arnold J was simply this: would claim 1 be obvious to a person skilled in the art having regard to the state of the art at the priority date? See *MedImmune Ltd v. Novartis Pharmaceuticals UK Ltd* [2012] EWCA Civ 1234 at [181] per Lewison LJ. Commercial, as well as technical, considerations may be relevant to that question; so may other factors, such as whether the step in the claim was obvious "to consider" or "to try" and whether there was "a motive to find a solution" to the problem addressed by the patent in suit.

31. In arriving at his fastidiously reasoned conclusion Arnold J considered and evaluated, in an orderly way, all of the evidence relevant to obviousness, including the evidence given by two experts on each side. Following the guidance in the authorities Arnold J addressed the evidence on obviousness in all its various aspects. Who was the notional person skilled in the art? What was the relevant common general knowledge of that person? What was the inventive concept of the claims? What differences, if any, were there between the state of the art and the inventive concepts? Were those differences steps which would have been obvious to the person skilled in the art? Or

did they require a degree of invention? Those are all aspects of the overwhelming question considered by the judge from every angle in the fact-finding process of evaluating the evidence.

32. The role of this court is not the same. The Court of Appeal does not retry the issue of obviousness. That has already been tried by Arnold J. This court reviews the case to see if the decision on obviousness is wrong. That issue involved the trial judge in an evaluation or assessment of the whole of the evidence, including the weight to be given to particular factors. This court is reluctant to interfere with a finding of obviousness, unless the judge has gone wrong on a point of legal principle or if, for some other reason, the decision is plainly wrong.

Obviousness: judgment below

33. In the course of his judgment Arnold J reached clear conclusions.

The skilled team and its leader

34. The judge recorded that there was little dispute by the end of the trial that the skilled person to whom the Patent is addressed is a team of people. It comprised a clinician, a pharmacologist, a formulation scientist and a pharmacokineticist. In a passage, which is said by AstraZeneca to be flawed by an error of principle, the judge said this:-

> "6. The only dispute between the parties was as to which member of the team should be regarded as the leader. The Claimants contend that the Patent is primarily directed to the formulator. AstraZeneca contends that the development of a new formulation of quetiapine would be primarily driven by clinical considerations and to that extent would be led by the clinician. The formulator would then use his knowledge and experience to try to prepare an appropriate formulation and method of manufacture for that formulation in accordance with the clinician's instructions as to what was required. In my judgment those contentions are not inconsistent with each other: AstraZeneca is looking at the position prior to the Patent, whereas the Claimants are looking at the position after the Patent. I therefore accept both contentions. Either way, as both sides accept, there would be a notional conversation between the members of the team, in which the advantages and disadvantages of potential formulations would be considered."

The common general knowledge

35. The judge recorded that, by the end of the trial, there was a good deal of common ground with regard to clinical common general knowledge and formulation common general knowledge. He set out the position regarding the basics of drug absorption and action [34]-[36]; immediate release formulations [37]-[39]; and sustained release formulations [40] and their advantages [42]. He reviewed the standard texts linking the use of sustained release formulations with improvements in compliance [[56]-[57].

36. Mr Daniel Alexander QC for the claimants explained that, although the judge found that sustained release formulations were a well known way to achieve a once-a-day formulation, sustained release is not a synonym for once-a-day; once-a-day can be immediate release or sustained release.

37. As regards the areas of common general knowledge that were in dispute Arnold J made a specific finding on compliance and convenience. That finding is challenged by AstraZeneca:-

> "64. …The conclusion which I draw from the evidence as a whole is that the perception of the skilled team would have been that once daily dosing was to be preferred to twice daily both because it might lead to better patient compliance, although there was no hard evidence that it did so, and because it was more convenient to patients and, particularly, carers. Furthermore, the skilled team would have been well aware that one of the advantages of sustained release formulations was that they enabled less frequent administration, and in particular once a day rather than twice a day."

38. In the light of the judge's findings I turn to Claim 1 in the Patent as analysed by the judge in [72]-[83].

The Patent

Claim 1: the inventive concept

39. There was no dispute about the construction of claim 1. The judge explained that the problem identified by the Patent was how to make a sustained release formulation: the inventive concept relates to "…a sustained release formulation of quetiapine comprising a gelling agent".

40. Paragraph [0002] of the specification itself recognises the general desirability for a sustained release formulation for more stable dosing and less frequent administration. It states:-

> "It is desirable in the treatment of a number of diseases, both therapeutically and prophylactically, to provide the active pharmaceutical ingredient in a sustained release form. Desirably the sustained release provides a generally uniform and constant rate of release over an extended period of time which achieves a stable and desired blood (plasma) level of the active ingredient without the need for frequent administration of the medicament."

41. The Patent went on to explain the numerous sustained release formulations known in the art utilizing gelling agents and the difficulties of formulating sustained release formulations of soluble medicaments and gelling agents [0003]; and the need for sustained release formulations of soluble medicaments such as quetiapine, which overcome or alleviate one or more of the described difficulties and allow the medicament to be administered less frequently, such as once a day.

42. The judge summarised the position by saying that the problems identified in the Patent, as being the problems to which the invention was addressed, were those identified in [0003]. The Patent then explained the invention by reference to a formulation comprising a gelling agent. The judge held that the values reported for the sustained release formulations were similar to those reported for the immediate release formulation [81].

Prior art-Gefvert

43. The pleaded prior art relied on is a short abstract published by Gefvert in September 1995. Gefvert did not disclose a *sustained* release formulation. The judge summarised what the Gefvert document, which considered dosage regimes of an *immediate* release formulation of quetiapine, would disclose to the skilled team [85]. Having considered the evidence of the experts, the judge made the following finding as to what the skilled team would conclude having read Gefvert:-

> "108. My conclusion from this evidence is that the skilled team would conclude from Gefvert that a single 450 mg dose of an immediate release formulation daily would not be efficacious. The skilled team would regard once daily administration as desirable for the reasons given in paragraph 64 above. (Incidentally, there is no evidence before me that sustained release quetiapine in fact has any other advantage.) To achieve once daily administration, a sustained release formulation and a higher dose of an immediate release formulation would both be obvious possibilities. "

44. It will be noted that the references to once-a-day not being efficacious is a reference to *immediate release* form dosed once a day, not to *any once a day formulation*.

45. It was not really disputed, the judge noted, that the skilled team would not consider developing a sustained release formulation of quetiapine, unless there was some clinical need or rationale for one.

46. In the light of the common general knowledge and in the light of Gefvert, Arnold J held that the inventive concept in claim 1 was obvious. He accepted the claimants' case that the skilled team would conclude from Gefvert that once daily dosing of 450mg of an immediate release formulation of quetiapine was unlikely to be efficacious; that the skilled team would consider that a sustained release formulation was likely to be efficacious and would offer advantages in terms of compliance and convenience and that the skilled team would expect to be able successfully to formulate a sustained release formulation of quetiapine using HPMC, which would be a routine choice of matrix and would in fact achieve success without difficulty. It would not expect from its common general knowledge nor conclude from the formulator's literature search that quetiapine was likely to saturate first pass metabolism.

47. The skilled team would not therefore be deterred from developing a sustained release formulation. Nor would its expectation of success be adversely affected.

The Dutch judgment

48. While expressing regret that Courts in different Member States have reached opposite conclusions about the validity of the same patent, the judge was not persuaded by the reasoning of the District Court of the Hague of 7 March 2012 that his conclusion was incorrect. He distinguished the Dutch decision on a number of grounds: different evidence; the Dutch court proceeded on the basis that the patent was not entitled to the priority date; different arguments were advanced; and different conclusions were reached on motivation and expectation of success.

AstraZeneca's grounds of appeal and submissions

49. Mr Simon Thorley QC submitted that the judge made errors of principle in concluding that claim 1 was invalid. The judge did not consider the allegations of obviousness on the basis advanced by the claimants in their evidence regarding the development of a new formulation of quetiapine starting from Gefvert and the clinician's reasons for recommending once-daily dosing in preference to twice-daily dosing and the requirement for those recommendations to be based on clinical considerations.

50. AstraZeneca appeals on the grounds that the judge misdirected himself on the role of the different members of the skilled team; that he made an error as to there being motivation for a once a day formulation; that he made an error in concerns over the effectiveness of a sustained release formulation; and that he made an error in his approach to the issue of obviousness .

51. As mentioned earlier, AstraZeneca does not pursue the appeal on claim 15. Nor does it pursue the point that the judge was wrong in principle to reach the conclusion that the skilled formulator would have approached the task of formulating quetiapine with a general expectation that its first pass metabolism would not be saturated by the clinical dose.

Skilled team point: role of different members

52. It is argued that Arnold J misdirected himself as to the *role* of the different members of the skilled team at different stages in the notional project. He held that, prior to reading the Patent, the clinician would lead the team and that, after reading the Patent, the formulator would lead the team.

53. It is contended that the judge was wrong to consider the position in the light of, or after reading, the Patent and that he should have held that the development of quetiapine would have been primarily led by the clinician, not by the formulator.

Motivation for once daily formulation

54. The next criticism is that the judge reached erroneous conclusions as to there being any motivation to the clinician to propose the development of a once-a-day formulation and on patient compliance and convenience. He was wrong to consider the convenience of a once-a-day dosing compared with a twice-daily regime. Convenience was not a reason for the clinician to recommend once daily dosing.

55. The judge was wrong to have regard to compliance from the formulator's perspective, as it had not been suggested that he would participate in the decision what dosage regime should be adopted. Clinicians varied in their opinions about daily dosing.

Failure to address totality of factors

56. It is submitted that the judge failed to address the totality of factors, which would have put the skilled team off, because of concerns about the development and effectiveness of a once-a-day sustained release formulation of quetiapine. He failed to consider AstraZeneca's case as a whole. Instead he took a step-by-step approach to the question of inventive step, considering each issue in the development process and rejecting each in turn.

57. The particular criticism is that the judge did not properly consider the totality of AstraZeneca's points on the key question of the skilled person's expectation of success in being able to make an improved formulation of quetiapine using sustained release technology. He adopted the impermissible stepwise approach in considering each stage or potential issue in the development process of sustained release formulation.

58. Arnold J was also said to be wrong in taking into account what the Patent stated to be problematical and what required invention. He should not have considered it significant that the problems identified in the Patent were illusory.

Discussion and conclusions

General

59. The legal principles have already been summarised. I agree with Mr Alexander QC that the issue of obviousness is quintessentially a matter of fact, degree and overall impression for the trial judge. His function was to evaluate the evidence as a whole and to reach a judgment on it. As Kitchin J put it in *Generics v. Lundbeck* [2007] RPC 32 at [72], which was later approved in *Conor v. Angiotech* [2008] RPC 28 :-

> "The question of obviousness must be considered on the facts of each case. The court must consider the weight to be attached to any particular factor in the light of all the relevant circumstances. These may include such matters as the motive to find a solution to the problem the patent addresses, the number and extent of the possible avenues of research, the effort in pursuing them and the expectation of success."

60. I also agree with Mr Alexander QC about the role of this court on an appeal against a finding of obviousness at trial. This court's function with regard to that issue is one of reviewing the conclusion to see whether there is any error of principle or some plainly wrong outcome. The function is not one of allowing the whole issue to be re-argued from scratch with a view to this court making a fresh evaluation of the evidence on what is a multi-factorial issue and in the expectation that a contrary determination of the merits of the issue would be substituted for the decision of the trial judge.

61. As indicated earlier, this appeal does not require the court to decide any novel point of law. Nor, in the light of the judge's findings and reasoning, does it present an appeal court with any special difficulties in applying settled law to the facts found at trial on the issue of obviousness.

62. Proceeding along a well trodden route, I will concentrate on the main grounds of appeal and briefly state my conclusions, while keeping an eye on the overall picture.

Skilled team membership: role of different members

63. I agree with Mr Alexander QC that AstraZeneca's criticisms about the notional skilled person are without substance. Arnold J did not misdirect himself on this aspect of obviousness.

64. In my judgment, the judge's description of the notional skilled person as a team was accurate and realistic. His assessment of obviousness was by reference to a notional team skilled in the prior art, as that notional team, without knowledge of the Patent, would have existed and operated. He made findings as to who would be in the team and as to how they would have interacted. That notional team would include a clinician, primarily involved pre-Patent, and a formulator, primarily involved post-Patent on the way sustained release formulation would be achieved. Those two roles would not, at different stages, be entirely separate, but would overlap and interact. The members of the notional team would not sit alone in separate rooms, come to their own final conclusion and then communicate it to other members of the team. Before coming to a conclusion they would notionally talk with one another about the issue. Thus, the dosage regimen desired for a formulation would not be for consideration by the clinician alone.

Motivation for once- daily formulation

65. This ground of appeal challenges as wrong the finding of fact made by the judge in [64] of the judgment quoted above, in which he concluded that the skilled team would perceive that once-daily dosing would obviously be preferred to twice-daily dosing: it might increase patient compliance.

66. Mr Thorley QC referred to selected extracts from the experts' evidence in support of this ground. Mr Alexander QC referred to selected extracts from the experts' evidence against that ground. This is a familiar and usually unproductive forensic ding-dong in furthering ambitious attempts to scale the heights necessary to persuade this court to interfere with findings of fact by the judge, who heard all the witnesses give their evidence. As Mr Thorley QC himself pointed out, in respect of Mr Alexander's use of part of the evidence given by one of AstraZeneca's experts (Professor Montgomery) on the issue of the obviousness of a sustained release formulation, the process of selecting extracts from the transcript of evidence given by a witness does not always create the same impression as hearing or reading the entirety of the evidence given by that witness.

67. In my judgment, the expert evidence and the relevant literature amply justified the judge's conclusion that the motivation for a more convenient once-a-day formulation was obvious at the priority date.

Failure to address factors regarding effectiveness of sustained release formulation

68. The original grounds of appeal stated that the judge was wrong to reach the conclusion that the skilled formulator would have approached the task of formulating quetiapine with a general expectation that its first pass metabolism would not be saturated by the clinical dose. That ground has been removed from the revised grounds without accepting that the judge's conclusion was correct. I do not therefore need to deal with the arguments on the first pass metabolism point.

Erroneous approach in law

69. Arnold J is criticised for his approach for taking an impermissible step-by- step approach and for taking into account what the Patent said was problematic and required invention.

70. I am satisfied that, overall, the judge did not adopt an impermissible analysis in the sense of taking suggested modifications to a piece of prior art and then proceeding step-by-step to find something obvious in the claim. In this case the sustained release formulation was achieved once one had the idea and the skilled person was not deterred for the various reasons suggested by AstraZeneca as to why it would not have been done. The analysis performed by the judge was the permissible one of addressing in a structured way the various reasons advanced by AstraZeneca as to why the sustained release formulation would not have been done.

71. In my judgment, the judge followed the correct approach to the issue of obviousness in addressing the arguments in a structured, orderly and logical way as applied to Claim 1. He rightly applied *Pozzoli Spa v. BDMO SA* [2007] EWCA Civ 588; [2007] FSR 37*; Johns-Manville Corp's Patent* [1967] RPC 479*;* and *Actavis UK Ltd v. Novartis AG* [2010] EWCA Civ 82; [2010] FSR 18.

72. As for the particular criticism that the judge was wrong to take account of what the Patent said was problematic and required invention, I agree with Mr Alexander QC that there was no error of legal approach and that, as an evidential matter, the judge was entitled to regard as significant what AstraZeneca had accepted as desirable, but now argued was not obvious.

Dutch decision.

73. The judge was rightly respectful in his discussion of the Dutch decision, which had been drawn to his notice as a judgment relating to the same Patent. However, it was a different case decided by different judges on the basis of different evidence and argument. Arnold J was neither bound by it nor was he obliged to justify his own judgment in the light of it.

Result

74. I would dismiss the appeal.

75. In brief, the decision of Arnold J on the obviousness of claim 1 was not wrong in principle nor was it plainly wrong for some other reason. There was ample evidence to underpin his assessment that claim 1 was obvious. His conclusion was justified on a proper application of his correct understanding of the relevant principles of patent

law to the facts found by him on the evidence. It is not the role of this court on the issue of obviousness to become embroiled in a detailed re-consideration of particular findings of fact for which there was some evidential basis.

Lord Justice McFarlane:

76. I agree.

Sir Terence Etherton:

77. I also agree.