Intellectual Property Office

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31 March 2016

PATENTS ACT 1977

BETWEEN

InterMune, Inc.	Proprietor
and	
Elkington and Fife LLP	Opponent

PROCEEDINGS

Request under section 74B of the Patents Act 1977 for a Review of Opinion 10/15 in respect of EP2124945

HEARING OFFICER Mrs S E Chalmers

DECISION

Introduction

1 This is a review of opinion 10/15 ("the Opinion") under section 74B of the Patents Act 1977 (the "Act") in respect of EP2124945 B1 ("the Patent"). The Opinion, which was requested by Elkington and Fife LLP ("the Opponent"), concluded that the patent lacked an inventive step.

2 The proprietor of the patent requested a review of the Opinion under section 74B of the Act and the opponent filed a counter statement contesting the application. Since neither party has asked to be heard, I have based my decision upon the papers currently on file.

The law

3 Reviews of opinions are provided for under section 74B. This reads so far as is relevant as follows:

> Rules may make provision for a review before the comptroller, on an application by the proprietor or an exclusive licensee of the patent in question, of an opinion under section 74A above.
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> (2) The rules may, in particular -
>
> (a) prescribe the circumstances in which, and the period within which, an application may be made;

4 Rule 98 of the Patents Rules 2007 sets out the grounds on which a review can be requested. It reads:

> (5) The application may be made on the following grounds only—
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> (a) that the opinion wrongly concluded that the patent in suit was invalid, or was invalid to a limited extent; or
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> (b) that, by reason of its interpretation of the specification of the patent in suit, the opinion wrongly concluded that a particular act did not or would not constitute an infringement of the patent.

5 The purpose and scope of a review under section 74B was clarified by Kitchen J in *DLP Limited*[1] where at paragraph 22 he stated:

> "In the case of an appeal under rule 77K [now Rule 100], the decision the subject of the appeal is itself a review of the opinion of the examiner. More specifically, it is a decision by the Hearing Officer as to whether or not the opinion of the examiner was wrong. I believe that a Hearing Officer, on review, and this court, on appeal, should be sensitive to the nature of this starting point. It was only an expression of an opinion, and one almost certainly reached on incomplete information. Upon considering any particular request, two different examiners may quite reasonably have different opinions. So also, there well may be opinions with which a Hearing Officer or a court would not agree but which cannot be characterised as wrong. Such opinions merely represent different views within a range within which reasonable people can differ. For these reasons I believe a Hearing Officer should only decide an opinion was wrong if the examiner has made an error of principle or reached a conclusion that is clearly wrong. Likewise, on appeal, this court should only reverse a decision of a Hearing Officer if he failed to recognise such an error or wrong conclusion in the opinion and so declined to set it aside. It is not the function of this court (nor is it that of the Hearing Officer) to express an opinion on the question the subject of the original request."

6 It follows that the remit of any review is quite narrow. It is not a rehearing to obtain a second opinion. Rather, I am required to review the opinion with a view to determining whether the examiner made errors of principle or reached conclusions that were clearly wrong, based on the material available at the time.

The patent

7 The patent relates to a specific escalating dosage regime to decrease adverse effects associated with pirfenidone (5-methyl-1-phenyl-2-(1H)-pyridone) therapy when used to treat idiopathic pulmonary fibrosis (IPF). These effects include gastrointestinal upset, nausea, fatigue, somnolence, dizziness, headaches and photosensitivity rash.

8 The patent has four claims:

> 1. Pirfenidone, in an initial dose escalation regimen, for use in treating idiopathic pulmonary fibrosis (IPF), wherein the pirfenidone is for: administering to a patient a first oral daily dosage of 801 mg as one capsule comprising 267 mg of pirfenidone three times a day for days one to seven of the dose escalation regimen; administering to the patient a second oral daily dosage of 1602 mg as two capsules comprising 267 mg of pirfenidone three times a day for days eight to fourteen of the dose escalation regimen; and administering to the patient a third oral daily dosage of 2403 mg as three capsules comprising 267 mg of pirfenidone three times a day for at least day fifteen of the dose escalation regimen; and wherein said dosages are for taking with food.

[1] DLP Limited [2007] EWHC 2669

2. Use of pirfenidone in the manufacture of a medicament for treating idiopathic pulmonary fibrosis (IPF), wherein the medicament is for: administering to a patient a first oral daily dosage of 801 mg as one capsule comprising 267 mg of pirfenidone three times a day for days one to seven of the dose escalation regimen; administering to the patient a second oral daily dosage of 1602 mg as two capsules comprising 267 mg of pirfenidone three times a day for days eight to fourteen of the dose escalation regimen; and administering to teh patient a third oral daily dosage of 2403 mg as three capsules comprising 267 mg of pirfenidone three times a day for at least day fifteen of the dose escalation regimen; and wherein said dosages are for taking with food.

3. A starter pack comprising: a first set of compartments each having a first dosage amount of pirfenidone that is 801 mg per day as one pill comprising 267 mg of pirfenidone three times a day; and a second set of compartments each having a second dosage amount of pirfenidone that is 1602 mg per day as two pills comprising 267 mg of pirfenidone three times a day; and at least one additional set of compartments each having a third dosage amount fo pirfenidone that is 2403 mg as three pills comprising 267 mg of pirfenidone three times a day, wherein the first set of compartments are for administering the first dosage amount of pirfenidone for Days 1, 2, 3, 4, 5, 6,and 7, and wherein the second set of compartments are for administering the second dosage amount of pirfenidone for Days 8, 9, 10, 11, 12, 13 and 14, and wherein the additional set of compartments are for administering a third dosage amount of pirfenidone beginning on Day 15.

4. The pirfenidone or use according to claim 1 or 2, wherein the initial dose escalation regimen reduces the incidence of an adverse effect associated with the administration of pirfenidone.

The Opinion

9 The Opinion found that the claims lacked an inventive step in view of prior art identified in the request and observations in reply, these being:

D1: M Selman et al., Drugs 2004 (64) 405-430

D2: OJ Dempsey, Respiratory Medicine (2006) 100 18710-1885

D4: S Nagai, Internal Medicine Vol 41, No 12 (202)

D5: TN Tozer and M Rowland, Introduction to Pharmacokinetics and Pharmodynamics, Baltimore, Lippincott Williams & Wilkins, 2006

D6: D Babovic-Vuksanovic et al, Neurology 2006 67 1860-1862

D7: A Gennaro, Ed, Remington: The Science and Practice of Pharmacy, 20ty Edition, Baltimore, Lippincott Williams & Wilkins, 2000

D8: G Downies, J Mackenzie and A Williams Eds, Pharmacology and Drug Managements for Nurses, 2nd edition, Edinburgh, Churchill Livingstone, 1999

D9: LM Shaw & TC Kwong, The Clinical Toxicology Laboratory, 2001 page 243

10 In its request for a review, the Proprietor challenges that finding on two grounds and asks for the Opinion to be set aside:

(a) the examiner erred in principle by misapplying the law on inventive step and supports that view with reference to a substantial body of case law and

(b) on the correct application of the law on inventive step, the Opinion would have found the patent to involve an inventive step.

11 The Proprietor also repeats the view stated in his observations that the examiner should have refused the request for an Opinion on the grounds that the request revisited issues already determined by the EPO. Whilst the EPO examiner did consider the question of inventiveness as part of the examination process, this does not bar the Opinion examiner from providing an opinion on obviousness on the basis of new documents. Nor does it prevent him considering documents cited in the substantive examination process before the EPO if he is satisfied that they raise new questions. The Opinion examiner concluded that the request for an opinion on the validity of the patent was allowable in part (paragraphs 5-11) and I agree with his assessment.

Arguments

12 The examiner discusses the question of obviousness in paragraphs 21-36 of his Opinion. He starts by setting out the well-established *Windsurfing/Pozzoli*[2] approach to obviousness. Both parties accept that is the right approach.

13 There does not appear to be any suggestion that the examiner erred in identifying the notional person skilled in the art. The Proprietor questions the examiner's view that D1, D2, D5, D6, D7, D8 and D9 are representative of the common general knowledge and asserts that there is no explanation why the skilled team would have viewed each as them as a reliable foundation for further work. However, he does not disagree that these documents would be known to the skilled person. In his view, only D4 is relevant as the closest prior art and this should act as the starting point for the analysis.

14 Step (1)(b) of the Windsurfing/Pozzoli test requires the examiner to identify the relevant common general knowledge (my emphasis) of the skilled person and he has done this. However, the examiner does not have the resources for expert evidence and cross-examination that are available to a court of law. Instead he has to make use of those documents before him. Paragraphs 25 and 26 of the Opinion set out the examiner's view why he considers all of these documents are relevant and I do not consider that he was clearly wrong in his assessment.

15 Both parties appear to accept the inventive concept as defined by the examiner in paragraph 20. There does not seem to be any suggestion that the examiner erred in identifying the difference between the "state of the art" and the inventive concept in the claims. It lies in the actual dosage regime that is defined in the claims which sets out a different rate of escalation of pirfenidone concentration and the final dosage given to the patient (paragraph 27).

16 Turning now to the fourth *Pozzoli* question, is the invention obvious? The Proprietor submits that the examiner erred in principle by adopting a "shorthand" approach to determining the question of inventive step. Specifically, in paragraphs 28 and 29 of the Opinion, the examiner interpreted what the Proprietor asserts are *obiter*

[2] Windsurfing Internationa Inc. V Tabur Marine (Great Britain) Lmd [1985] RPC 59A as restated and elaborated upon in Pozzoli SPA v BDMO SA [2007]EWCA Civ 588

comments in the Court of Appeal judgment in *Actavis v Merck*[3] as setting out a "special test" for assessing the inventive step of claims to dosage regimes, namely requiring the existence in the prior art of a clear factual prejudice against a claimed dosage regime before it can be found to be inventive. In effect, the Proprietor says the examiner is effectively starting from a presumption of invalidity.

17 He argues that this approach is not correct; the obviousness of a dosage regime should not be assessed using a different test to any other type of claim. In short, paragraph 29 of *Activis v Merck* relates to an aside in a section of the judgment relating to novelty (which was the issue under consideration) and the comments cannot be considered to be binding precedent for deciding obviousness. Rather, a multifactorial enquiry is required taking into account all relevant factors in the circumstances of the particular case to answer the statutory question of whether or not the claimed dosage is obvious.

18 The Proprietor supports his view with reference to a substantial body of case law. In particular, he stresses that recent cases concerned with claims to dosage regimes have not applied a "special test" based on *Activis v Merck* but have considered obviousness from first principles. As Kitchen J said in *Generics (UK) Ltd v H Lundbeck A/S*[4] and approved by the House of Lords in *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc*[5]:

> "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 involved in pursuing them and the expectation of success."

19 With regard to the statutory question, the Proprietor cites the Court of Appeal decision in *Activis v Novartis*[6] in which Jacob LJ says:

> "at bottom the question is simply whether the invention is obvious. Any paraphrase or other test is only an aid to answering the statutory question."

20 Similarly, in the Court of Appeal in *Medimmune v Novartis*[7], Kitchen LJ said:

> Ultimately the Court has to evaluate all the relevant circumstances in order to answer a single and relatively simple question of fact: was it obvious to the skilled but unimaginative addressee to make a product or carry out a process falling within the claim. As Aldous LJ said in Norton Healthcare v Beecham Group Plc (nreported, 19 June 1997):
>
> "Each case depends upon the invention and the surrounding facts. No formula can be substituted for the words of the statute. In every case the Court has to weigh up the evidence and decide whether the invention was obvious. This is the statutory task."

21 The Proprietor also cites a number of other judgments[8] to support his argument that the comments in *Activis v Merck* are not binding – specifically in relation to a

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[3] Activis UK Limited v Merck & Co Inc [2008] EWCA Civ 344
[4] Generics (UK) Ltd v H Lundbeck A/S [2007] EWHC 1040 (Pat)
[5] Conor Medsystems Inc v Angiotech Pharmaceuticals Inc [2008] UKHL 49
[6] Activis UK Limited v Novartis AG [2010] EWCA Civ 82
[7] Medimmune Limited v Novartis Pharmaceuticals UK Limited and other [2012] EWCA Civ 1234
[8] Hospira UK Limited v Genentech Ic. [2014] EWHC 1094 (Pat); Hospira UK Limited v Genentech Inc [2015] EWCA Civ 57; Generics (UK) Limited (trading as Mylan) v Richter Gedeion Vegyeszeti Gyar

requirement of prejudice – when considering dosage regimes. In particular, he notes that none of these judgments reference paragraph 29 of *Activis v Merck* and argues this is strongly indicative that it is not the binding authority as the examiner understood it to be.

22 He also cites a number of EPO decisions to further underline his point about a requirement of prejudice when considering inventive step in relation to dosage regimes. I do not propose to cite them all here; however, I note the Proprietor's reference to *HGS v Eli Lilly*[9] where the Supreme Court held, as a consequence of the need for UK patent law to be aligned with EPO jurisprudence as far as possible that:

> "where the Board [ie EPO Board of Appeal] has adopted a consistent approach to an issue in a number of decision, it would require very unusual facts to justify a national court not following that approach."

23 Unsurprisingly, the Opponent disagrees. He submits that, far from using a "special test", the examiner clearly set out his assessment of inventive step using the established 4-step test of *Pozzoli*. In asking the final question, he correctly used a multi-factorial assessment, as set out in paragraphs 30-37, which is fully in line with the case law referenced by the Proprietor. The Opponent submits that the Proprietor has misunderstood the examiner's reference to *Activis v Merck* and has overstated its influence on the Opinion to assert that the examiner asked himself only the question of whether a technical prejudice existed. He points out that the comments were made by a Court of Appeal judge setting out the legal and technical background of the case where the judge made a statement of fact ie it is standard practice to investigate appropriate dosage regimes. He says that it is irrelevant whether the comments are *obiter* or otherwise, or whether they are binding or non-binding. He therefore submits that there are no grounds for a review of the Opinion based on the approach of the examiner.

Is there an error of principle?

24 The law is clear that the question of obviousness must be considered on the facts of each case and that the weight to be attached to any particular factor must be considered in the light of all the relevant circumstances. Set against that is the fact that an Opinion is not based on the outcome of fully litigated proceedings. It is necessarily based on whatever material is placed before the examiner, however incomplete that may be.

25 I start by saying that I do not believe the examiner made an "error in principle" by including technical prejudice *per se* in his analysis as that can be a relevant factor when assessing obviousness in any technical field. I shall now consider the examiner's interpretation of the comments in *Activis v Merck*.

26 The Opinion at paragraph 29 states "the Court further made clear that there is a presumption that a new dosage regime will not be inventive unless there is a clear technical prejudice pointing away from the dosage regime." (I observe that this

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RT [2014] EWHC 1666 (Pat); Hospira UK Limited and others v Novartis AG [2013] EWHC 516 (Pat); Novartis AG and others v Focus Pharmaceuticals Limited and others [2015] EWHC 1068 (Pat)

[9] Human Genome Sciences Inc v Eli Lilly and Company [2011] UKSC 51

statement appears to reference the IPO's guidelines for examining medical inventions[10].) The Opinion then goes on to quote Paragraph 32 of *Activis v Merck* which reads:

> "So holding is far from saying that in general just specifying a new dosage regime in a Swiss form claim can give rise to a valid patent. On the contrary nearly always such dosage regimes will be obvious – it is standard practice to investigate appropriate dosage regimes. Only in an unusual case such as the present (where ... treatment for the condition with the substance had ceased to be worth investigating with any dosage regime) could specifying a dosage regime as part of the therapeutic use confer validity on an otherwise invalid claim."

27 My reading of this passage is that it provides useful guidance on determining obviousness in saying that it is standard practice to investigate appropriate dosage regimes and that only in an unusual case could specifying a dosage regime confer validity on an otherwise invalid claim. Although the *Activis v Merck* judgment held the patent was non-obvious on the basis of overcoming a technical prejudice, I struggle to see how the passage quoted above leads to the general presumption that there must be a clear technical prejudice (my emphasis) pointing away from the dosage regime to confer validity. In coming to this view, I find support in the approach to obviousness taken in the body of case law cited by the Opponent. I therefore find that the examiner did make an error in principle in taking this approach as his starting point.

28 However, I am satisfied that, in coming to his opinion, the examiner did carry out a multifactorial assessment based on the material before him as far as he was able. These factors took into account:

(i) the technical contribution made by the patent although he notes there is no evidence in the patent to show that the escalating dosage regime claimed does have the advantages and outcomes asserted (paragraphs 30-33);

(ii) the standard practice for the skilled team in these cases ie to investigate appropriate dosage regimes (paragraph 36);

(iii) what the common general knowledge shows ie that escalating dosage regimes can be adjusted to minimise adverse effects (paragraph 36); and

(iv) whether there was any technical prejudice against the claimed dosage (paragraphs 35 and 37).

29 Given that the Opinion examiner applied the established 4-step test for obviousness and carried out the required multi-factorial analysis, I do not consider his overall approach amounts to an error in principle.

Does the patent involve an inventive step?

30 The patent suggests that adverse effects are alleviated by dose reduction or discontinuation, referencing a recent study[11] by *Azuma et al* in which the dosage

[10] Examination Guidelines for Patent Applications relating to Medical Inventions in the Intellectual Property Office, paragraph 114 (May 2013) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/315048/medicalguidelines.pdf

was reduced in a stepwise manner, and, where if the adverse reactions continued, the study medication was discontinued. The patent also states that *Azuma et al* discloses a dose titration schedule wherein the patients received a 200mg dose of pirfenidone three times a day for the first two days' a 400mg dose three times a day for the following two days; and the maximum 600 mg dose three times a day for the remaining treatment. The patent suggests that this dose escalation regime does not optimally match the rate at which a patient develops tolerance to reduce adverse effects, and that the maximum dose obtained is only 1800 mg per day, such that there remains an unmet clinical need for a method to administer higher doses of pirfenidone to a patient that minimizes or eliminates adverse effects.

31 The Proprietor's arguments restate and generally expand on their observations on why the claimed invention is inventive. I note that these arguments in part revisit documents previously considered by the EPO examiner in relation to technical contribution and plausibility and are hence outside the scope of the Opinion (paragraphs 9, 10 and 30 refer) and this review. They also introduce new lines of argument, for example in relation to D4, which also lie outside the scope of this review as they add to the material available to the examiner.

32 The Proprietor submits that, on the basis of document D4, there is no evidence to motivate the skilled team to change the prior art dosage regime to arrive at the claimed dosage regime nor that there is any evidence of a fair expectation of success in reducing the incidence of adverse effects. He argues that the skilled person would not have been motivated to investigate other dosage regimes, because the teaching of D4 is temporarily to discontinue and reinstate treatment in the case of photosensitivity problems.

33 The Opponent argues that, in general clinical practice, there is always the motivation to find a dosage regime with which there would be no need for discontinuation of treatment to reduce side effects. He says that the clinician specialising in the field of fibrosis and pharmokinetics would therefore be highly motivated to develop a dosage regime resulting in reduced adverse reactions without having to interrupt treatment. He also makes the point that simply because a prior art document offers one solution to a problem does not lead to the conclusion that the skilled person would not seek an improved solution. This is all the more desirable when the solution offered by the prior art – discontinuation of treatment – is far from ideal.

34 With respect to the technical contribution, the Proprietor repeats arguments that the EPO was satisfied that the invention is plausible and the Opinion examiner has correctly, in my view, considered this issue is outside the scope of the opinion. The Opponent notes that the examiner concluded (paragraph 32 of the Opinion) that the assertion that the claimed dosage regime results in a decrease in adverse effects had not been demonstrated and argues that it is simply arbitrary. The Opponent further notes there are no examples in the patent itself and the post-published clinical trial data only compare the claimed dosage regime with placebo. There is no comparison with an existing dosage escalation regime eg D4.

35 The Opponent rebuts the Proprietor's statement that the examiner did not take into account the expectation of success the skilled person would have in modifying the

[11] A Azuma et al, Am J Respir Crit Care Med 171:1040

dosage regime by simply saying that the examiner took the view that no effect had been demonstrated by the claimed dosage regime. It is merely arbitrary and he submits that it would be wrong to require a fair expectation of success, in terms of reducing adverse events, if no reduction in adverse events had been demonstrated by the claimed dosage regime. The expectation required is merely that the claimed dosage regime is suitable for treating IPF which, he says, is plainly the case.

36 This leads me to the final consideration of whether the cited prior art supports a case that the invention is obvious. The Opinion concluded that it did. In particular, paragraph 25 says that "the clinician who is a specialist in fibrosis would be aware of the teaching of documents D1, D2 (and D6) concerning trials on the use of pirfenidone in the treatment of IPF" and that "escalating dosage regimes are known in the art and have been used with a wide range of medicines especially when there is a need to avoid adverse reactions" – this is shown in D5 and D9. In paragraph 32, the examiner notes there is no evidence in the patent to support the assertion that the claimed dosage regime results in a decrease in adverse effects. Paragraph 36 states that "escalating dosage regimes are not only known, but can be adjusted as part of routine practice to achieve a desired dosage while minimising adverse effects."

37 I am satisfied that the examiner's assessment of these documents was reasonable and that he correctly viewed these in combination as representative of the common general knowledge. As a result, I am of the view that – based on the material before him – the examiner was not clearly wrong in his conclusion that the skilled team would investigate escalating the dosage regimen to arrive at the desired final daily dosage using their general knowledge about such regimens and the drug pirfenidone in particular.

Conclusion

38 I conclude that the examiner did not reach an opinion in Opinion 10/15 that was clearly wrong. He did, in my view, make an error in taking as his starting point the presumption that a new dosage regime will not be inventive unless there is a clear technical prejudice pointing away from the dosage regime. However, I do not consider that sufficient to set the Opinion aside.

Appeal

39 Any appeal must be lodged within 28 days after the date of this decision.

Mrs S E Chalmers

Deputy Director acting for the Comptroller