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Case No: HP-2014-000040

HP-2015-000012, HP-2015-000048 and

HP-2015-000062

IN THE HIGH COURT OF JUSTICE

**BUSINESS AND PROPERTY COURTS OF ENGLAND AND WALES**

**INTELLECTUAL PROPERTY (ChD)**

**PATENTS COURT**

**Appeal Refs: 2016/4110, 4094, 4104** Royal Courts of Justice

The Rolls Building

7 Rolls Buildings

London, EC4A 1NL

Date: 10/11/2017

**Before**:

MR. JUSTICE HENRY CARR

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**Between:**

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| **ACTAVIS GROUP PTC EHF**  **(a company incorporated under the laws of Iceland)**  **Claimant in HP-2014-00004-/Appellant**  **ACTAVIS UK LIMITED**  **Fourth Party in HP-2014-000040/Appellant**  **TEVA UK LIMITED**  **TEVA PHARMACEUTICAL INDUSTRIES LIMITED**  **(a company incorporated under the laws of Israel)**  **Claimants in HP-2015-000048/Appellants**  **GENERICS (UK) LIMITED (t/a MYLAN)**  **Claimant in HP-2015-000062/Appellant** |
| **- and -** |
| **ICOS CORPORATION**  **(a company incorporated under the laws of the State of Washington, USA)**  **Defendant/Respondent**  **ELI LILLY AND COMPANY**  **(a company incorporated under the laws of the State of Indiana, USA)**  **Third Party** |

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**MR. ADRIAN SPECK QC** and **MR. THOMAS JONES (**instructed by **Bird &**

**Bird LLP)** appeared for **Actavis Group PTC EHF,** and (instructed by **Taylor Wessing LLP)** appeared for **Generics (UK) Limited (trading as Mylan)** and (instructed by **Pinsent Masons LLP)** appeared for **Teva Pharmaceutical Industries.**

**DR. JUSTIN TURNER QC** and **MS. KATHERINE MOGGRIDGE (**instructed by

**Allen & Overy LLP)** appeared on behalf of **ICOS** and **Eli Lilly.**

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Approved Judgment

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**MR. JUSTICE HENRY CARR:**

**Introduction**

1. This is an urgent application by the Defendant and Third Party (“Lilly”) for an interim injunction to stop the launch by the claimants, three well‑known generic organisations, of 2.5 mg and 5 mg generic tadalafil for daily use for the treatment of erectile dysfunction (“ED”). The launch is schedule for Monday 13th November. On the same date, the SPC which protects 10 and 20 mg tadalafil for on demand use for ED will expire and generic equivalents will be launched.
2. The background is that by a judgment dated 1st November 2017, [2017] EWCA Civ 1671 the Court of Appeal overturned a finding by Birss J that the patent in suit, which protected the 5 mg or less daily dosage regimen, was inventive. The Court of Appeal gave permission to Lilly to apply to the Patents Court for interim injunctive relief, pending determination of its application for permission to appeal to the Supreme Court. Lilly is currently petitioning the Supreme Court for permission to appeal. That application is unlikely to be determined for some months.
3. It may seem counterintuitive to consider injunctive relief in respect of a patent which has been held to be invalid. However, where an appeal is pending which has a real prospect of success, the inquiry is more complex than might appear at first sight. The court is attempting to preserve the position so that if an appeal is successful, the appellant will not be deprived of the fruits of the appeal; or even if the appeal is not rendered nugatory, will not suffer greater harm which cannot be compensated in damages than the unsuccessful respondent.
4. In *Novartis v Hospira* [2013] EWCA Civ 583; [2014] 1 WLR 1264 Floyd LJ summarised the principles to be applied when considering interim injunctive relief pending appeal at [41], which I shall apply in the present case:

“i) The court must be satisfied that the appeal has a real prospect of success.

ii) If the court is satisfied that there is a real prospect of success on appeal, it will not usually be useful to attempt to form a view as to how much stronger the prospects of appeal are, or to attempt to give weight to that view in assessing the balance of convenience.

iii) It does not follow automatically from the fact that an interim injunction has or would have been granted pre-trial that an injunction pending appeal should be granted. The court must assess all the relevant circumstances following judgment, including the period of time before any appeal is likely to be heard and the balance of hardship to each party if an injunction is refused or granted.

iv) The grant of an injunction is not limited to the case where its refusal would render an appeal nugatory. Such a case merely represents the extreme end of a spectrum of possible factual situations in which the injustice to one side is balanced against the injustice to the other.

v) As in the case of the stay of a permanent injunction which would otherwise be granted to a successful claimant, the court should endeavour to arrange matters so that the Court of Appeal is best able to do justice between the parties once the appeal has been heard.”

**Real prospect of success**

1. In contrast to the position of the appellant in *Novartis v Hospira*, Lilly has not been granted permission to appeal. The Court of Appeal has refused permission on the basis that the case does not raise a point of law of general public importance. From Lilly’s perspective, any appeal is a hope which has not yet been realised. In those circumstances, it is common ground I have the unusual task, for a first instance judge, of deciding for the purposes of this application whether the application for permission to appeal, and any subsequent appeal to the Supreme Court has a real prospect of success.
2. Dr. Turner, who argued this case with considerable skill on behalf of Lilly, submitted that the Court of Appeal has fallen into error on an important point of law. He said that the court should have asked itself two questions. First, was it obvious that a dose of 5 mg or less of tadalafil taken once daily would be efficacious for the treatment of erectile dysfunction at the priority date from the prior art read in the light of common general knowledge. Secondly, was it obvious to try this dosing regimen for this therapeutic purpose at the priority date with a reasonable prospect of success. Both of those questions are to be judged at the priority date, and not in the light of information subsequently obtained. If the answer to both questions is no, as in the present case, then the patent is inventive. Dr. Turner submitted the Court of Appeal fell into an error, which the judge at first instance did not make, by postulating a series of clinical trials, the results of which would then lead to a further clinical trial; the ultimate result of which would be to test the claimed dosage regimen of tadalafil, but even then, without a realistic prospect that it would be sufficiently efficacious to treat ED.
3. At [133] of his judgment in the present case Kitchin LJ referred to the guidance given by the Court of Appeal as to the relevance of whether a route was obvious to try and the skilled team's expectation of success in *Novartis AG v Generics UK Limited* *(trading as Mylan)* [2012] EWCA Civ 1623. In particular, he referred to paragraph 55 of that judgment, where he said:

"I of course accept that a patentee is entitled to have the issue of obviousness assessed by reference to the invention he has described and claimed. This was made clear by Lord Hoffmann in Conor at [19]. In deciding whether the invention was obvious to the skilled but unimaginative addressee at the priority date the court will have regard to all the circumstances of the case including, where appropriate, whether it was obvious to try a particular route with a reasonable or fair expectation of success. What is a reasonable or fair expectation of success will again depend upon all the circumstances and will vary from case to case. Sometimes, as in Saint Gobain, it may be appropriate to consider whether it is more or less self‑evident that what is being tested ought to work. So, as this court explained in that case, simply including something in a research project in the hope that something might turn up is unlikely to be enough. But I reject the submission that the court can only make a finding of obviousness where it is manifest that a test ought to work. That would be to impose a straightjacket upon the assessment of obviousness which is not warranted by the statutory test and would, for example, preclude a finding of obviousness in a case where the results of an entirely routine test are unpredictable." (emphasis added).

That statement of law, which is very well established, includes the proposition that where the results of an entirely routine test are unpredictable, nonetheless there may be a finding of obviousness. It is not inventive to carry out a routine test, and if the test results in an unexpected bonus, it is still not an invention. If this appeal is to succeed, that proposition needs to be successfully challenged.

1. Kitchin, Floyd and Lewison LJ gave separate judgments setting out why they considered that the appeal should be allowed. For present purposes, I shall refer to the judgment of Floyd LJ at [163] ‑ [171]. An important finding of the judge was that, as part of a routine Phase IIb dose ranging study, it was very likely that 5 mg at a daily dosage would be tested. Floyd LJ also noted that the judge found that the skilled team, when carrying out a test of 5 mg dose per day of tadalafil would not have had a reasonable expectation that the drug at this dose would be a useful treatment for erectile dysfunction, nor any expectation that the drug would produce a clinically relevant effect but with minimal side effects.
2. However, that would not be the object of the dose ranging study. The object of the study would not be to find a minimum effective dose, but to identify a dose response, and the discovery of a plateau meant that the study would have to be repeated at a lower dose to enable it to be completed. Floyd LJ identified what the Court of Appeal regarded as the judge’s error at [168] – [171]:

“168 Overall, the judge considered that the team would embark on the project with a reasonable expectation of success in establishing tadalafil as a safe, tolerable and effective treatment for tadalafil. However, the claimants had failed to prove that efficacy at 5mg tadalafil was predictable or worth considering by the skilled team based on the properties of tadalafil as compared to sildenafil. The team would know that in principle there would be a minimum effective dose for tadalafil but would also know that its definition depends on a value judgment made by the team. In relation to the dose ranging studies, the team would conduct them hoping for a dose response. Following discovery of a plateau starting at 25 mg or 10mg, there would "very likely" be a subsequent dose ranging study which included 5 mg. The team would include a 5 mg dose in this study hoping to see a dose response but that does not mean they would have a reasonable expectation that 5mg would produce a clinically relevant effect at all nor one with minimal side effects. Assuming a 5 mg /day dose of tadalafil was tested, it would not be tested with a reasonable expectation of success. The result for the 5 mg/day dose was a surprising one: the existence of a useful effect with reduced side effects. A number of value judgments would be required of a skilled team in a programme which reaches the claimed invention. One was to define the level of clinical effect to be regarded as relevant. Another was to embark on investigating daily dosing. An important value judgment was what to do when an unexpected plateau in the dose response has been identified at the same time as a marketable dose.

169 I think that it was in these final steps in his reasoning that the judge fell into error. The whole purpose of embarking on the routine Phase IIb dose ranging study was to identify a dose response. The discovery of a plateau indicated that the routine study would have to be repeated at a lower dose, because it was not complete. Completion of the study would inevitably lead the skilled team to test 5 mg/day, whether that dose was still on the plateau, or in a region of the curve where a dose effect is observed. Which it is does not matter, because the result is that the skilled person would at this stage have arrived at a dosing regimen within the claim.

170 Whilst the existence of value judgments on the road to the invention are of course highly material, the judgments identified by the judge in this passage of his reasoning were collateral ones which had no impact on the decision to complete the Phase IIb study, or were not true value judgments at all. Thus the judge relied on the need to define the level of clinical effect to be regarded as relevant, i.e. the minimum effective dose. The identification of a dose response and the identification of a minimum effective dose are, however, different things. The need to complete the Phase IIb study and identify a dose response does not involve exercising a judgment about minimum effective dose. Likewise, if by referring to the decision to embark on investigating daily dosing the judge was intending to refer to chronic daily dosing, that is also not an obstacle to completing the Phase IIb trial with the 5 mg maximum daily dose and arriving within the claim by that route. Finally, the judge relied on the decision as to what to do when faced with the plateau. There was ample evidence to suggest that, far from being a value judgment, investigating lower doses was something the skilled team would do without further thought.

171 I think the judge also allowed himself to be side-tracked by his undoubtedly correct conclusion that the skilled team would not have been able to predict that the 5 mg/day dose would be effective. If the only thing which was driving the skilled team to test the 5 mg dose was its level of expectation that a 5 mg dose might be effective, the judge's conclusion about expectation of success as to efficacy would be highly material. The skilled team does not generally undertake steps with a given objective in mind without a reasonable expectation of success in obtaining that objective. Phase IIb tests are, however, conducted with a separate objective, namely to identify a dose response. The judge rightly held that it is very likely that these routine tests would be conducted for precisely that reason. Indeed that is the only basis on which his conclusion that the skilled person was very likely to do such tests is understandable. The absence of an expectation of success as to efficacy is, in these particular circumstances, not relevant.”

1. As a result of taking an entirely routine step, which the judge had concluded was very likely, and therefore obvious, the skilled person would perform an act falling within the claims of the patent. Floyd LJ concluded at [172] that: *“It is true that the judge made a finding that the skilled team would be surprised by the result, namely efficacy at 5 mg/day. However it is a result which on his findings would be arrived at by the standard, routine enquiries into dose response which are required by Phase IIb clinical trials. The surprising result, once uncovered, does not make these routine enquiries inventive.*”
2. In my judgment, there is no realistic prospect that this appeal will succeed. The judgment is an application by the Court of Appeal of the facts as found by the judge to existing and settled principles of law. Therefore, I do not consider that this application for an interim injunction crosses the first hurdle of a realistic prospect of success.
3. However, I do not rest my decision on that basis alone. In case I am wrong, I will consider unquantifiable harm to the parties, all of whom are able to pay any damages which the court may subsequently award.

**Unquantifiable loss to Lilly if the injunction is refused**

1. Lilly's case was a familiar one in battles between pharmaceuticals and generics. If an injunction is refused the price of 5 mg and 2.5 mg per day tadalafil will spiral downwards, most likely to only 10% of its existing price, a proposition which is borne out by what happened when Viagra became generic. That is not contested by the Claimants, who accept that the price will spiral downwards.
2. Lilly's next proposition is that when the price spirals downwards, it will be faced with two alternatives; either to maintain the current branded price, and save what part of the market it can based on brand loyalty and sacrifice the rest; or, alternatively, to compete on price. Both alternatives, it submits, will cause unquantifiable harm because either it will lose virtually all of the market or it will not be possible to put the price back up if the monopoly is restored. Lilly points out that this has been recognised by the courts in previous cases as significant unquantifiable harm.
3. There are certain aspects of this case which are different from other cases to which Lilly has referred. First, if the appeal to the Supreme Court is successful, the patent will only have a short period before it expires. The recent, well known case of *Actavis* *v Lilly* took two years one month from filing of the petition to the Supreme Court to judgment. In the present case, the patent will expire in April 2020. A similar period before judgment would mean that it would have less than six months before expiry. So discussion of a price rise during a period of restored monopoly is limited to a very short period. This does not create the difficulty of predicting changing market conditions where a patent has several years of monopoly.
4. Secondly, Lilly's prices for this particular dosage regimen per pack are fixed. There is no price reduction that is suggested in the evidence and Lilly do not, for example, reduce its prices to try to compete with parallel importers. On any damages inquiry, the price at which Lilly would have sold the patented product during the next few years will be known.
5. Third, the market for this dosage form, although the product is very successful, is flat; by which I mean it is settled both in value and quantity of packs. Sales were about £18 million over the last two years since introduction.
6. Turning to the first alternative contemplated by Lilly, where it maintains its price, any damages inquiry will be heard after the patent has expired. Mr. Speck accepts that every sale made by the generic companies will be a sale lost to Lilly, so that is precisely quantifiable. In terms of the amount of lost profit per sale, that can be calculated by reference to the fixed price currently charged by Lilly.
7. Dr. Turner was understandably concerned that it might be argued that because of the sales which are about to start of generic tadalafil in 10 and 20 mg on‑demand dosages, the Claimants might say the price of the lower daily dose would have fallen in any event. Mr. Speck, on instructions, has confirmed that this point would not be argued on any damages inquiry. Therefore, from Lilly's perspective, the enquiry, if it happens, would be extremely simple. In my judgment, Lilly has not established that it will suffer unquantifiable damage. Therefore, the injunction application fails for this reason as well.

**Unquantifiable loss to the Claimants**

1. If I am wrong about that, and Lilly is able to establish some unquantifiable loss, it appears to me that the unquantifiable loss to the Claimants, if an injunction were granted, considerably outweighs any unquantifiable loss to Lilly. This is because the Claimants find themselves in the position of what Mr. Speck has described as ‘first movers’. That does not mean that one company will be first to the market, but rather that all three will be early to the market. The evidence suggests that when a generic company supplies a wholesaler, that wholesaler is likely to stick with that generic company. If the generic company is in early and establishes the first sales, that is likely to continue. Later entrants to the market are much less likely to make serious inroads. Therefore, it is very important to these claimants (although they may be in competition with others as well) to be able to launch as soon as possible.
2. If an injunction were granted in two years' time, it is clearly foreseeable that there will be many other generic entrants to the market who, by that stage, will have obtained their own market authorisations. Therefore, the market conditions will be entirely different. That means the sales of this particular product will be difficult to quantify, and also that the sales of other products in the portfolio, which are sold in bundles, will be difficult to quantify. It will also be difficult to compare marketing initiatives, and volume discounts which the generic companies would, at that stage, be required to apply in order to sell the products with the current market conditions. Therefore, I consider that if I did grant the injunction, the Claimants’ loss would be very difficult to quantify.

**Public interest considerations**

1. Mr Speck also made two public interest points:

i) Generic manufacturers already had to start proceedings about two and a half years before launch in order to clear the way of patent protection, allowing for an appeal to the Court of appeal. It would be impractical to extend this period to five years to allow for the rare case of an appeal to the Supreme Court. This would be contrary to the public interest as it would discourage generic manufacturers from entering the market, which benefited the public by making available lower cost medicines.

ii) There is a public interest in obtaining lower cost medicines. Even though a cross undertaking in damages could be extended to the health services, recovery would be costly and would never be 100%.

1. As to the first point, ‘clearing the way’ is only one factor to be considered in the grant or refusal of interim relief, and the weight to be attached to it (if any) would be likely to be much less in the case of a second-tier appeal. As to the second point, this would apply to every case where an injunction is granted to restrain infringement of a pharmaceutical patent. There is also a public interest in encouraging and rewarding pharmaceutical research by enforcement of patents. In reaching my conclusion, I have not relied on either of these public interest points.

**Conclusion**

1. For these reasons, I refuse to grant the injunction.

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