GOWLING WLG

ELI LILLY V HUMAN GENOME SCIENCES: A CASE OF WHAT IS IMPLICITLY, BUT NECESSARILY AND SPECIFICALLY IN POINT!

10 January 2015

This article was previously published in the January 2015 edition of the CIPA

Don't be fooled by the fact that this is a case about supplementary protection certificates (SPCs) - it is more than that. Patent attorneys learn in the nursery that, if it is an invention, it is entitled to protection for an invention. That is independently of the size of the invention; and without regard to whether the leap arose from a five-minute chat in the coffee bar or years of research and investment; a compromise based on the simplicity of the result.

This means that some inventions seem to get too much protection - innovations in IT which would always have been overtaken in a year or two; and some receive too little - like pharmaceuticals which take years to get to market. Later, patent attorneys learn to fear the hand of the Court of Justice of the European Union (CJEU); it can make things even more complicated with Delphic pronouncements on very specific cases. Both these topics should be close to every patent attorney's heart; the latter particularly as CIPA has striven with other professional groups to keep patents away from the CJEU.

The former because, ultimately, whether inventions as a whole receive protection commensurate with their contribution, affects how politically acceptable patents are. SPCs were supposed to mend (or at least ameliorate) the first problem by giving extended protection for some pharmaceutical products.

Tom Carver examines how, in Eli Lilly v Human Genome Sciences (2014) that hasn't quite worked: here the patent owner obtains the benefit of a third party developing a commercial product. First though, he looks at Mr Justice Warren's analysis of the typically, but perhaps unhelpfully, cryptic pronouncement from the CJEU that an SPC is justified when "the claims [of the patent] relate, implicitly but necessarily and specifically,

to the active ingredient in question" and that it is for the national court to decide whether that is the case, and he offers some suggestions as what this might mean.

Introduction

The case between Eli Lilly and Human Genome Sciences (HGS), in which Lilly sought a declaration that any Supplementary Protection Certificate (SPC) applied for by HGS on the basis of EP (UK) 0 939 804 (owned by HGS) and Lilly's marketing authorisation for its antibody tabalumab would be invalid, has settled. This is a shame for those of us who agreed with Warren J that the judgment of the CJEU "failed to give [the] court the clear guidance that it hoped for"[1] and were looking forward to the Court of Appeal's interpretation of the CJEU's musings.

To recap: HGS's '804 patent was held in prior proceedings to be valid, but to contain very little useful information. Jacob LJ, in the appeal judgment[2], quoted Mr Thorley (HGS's counsel) as saying, "... [the skilled person] would know that no such [pharmaceutical or diagnostic] compositions had been disclosed and that what the patentee had discovered and disclosed is neutrokine-α and its antibodies with a practical use for these purposes yet to be discovered. So there is no reason to suppose that in these claims the patentee intended any specific application for the claimed compositions". Lewison LJ commented[3] that "It is clear from the specification that the patentee had no real idea what neutrokine-α or its antibodies would do if introduced into a living creature...". The '804 patent is due to expire in October 2016. HGS has developed its own antibody to neutrokine-α, belimumab, and has obtained patent and SPC protection for it. Lilly was developing an antibody (tabalumab) which it conceded would have infringed the broad antibody claims of the patent (which claimed all antibodies to neutrokine-α) and was concerned that HGS would engage in what has become known as 'SPC squatting'.

A patentee may apply for an SPC for a particular product, and, whilst the matter is contentious[4], the patentee can seek to do so on the basis of a marketing authorisation obtained by a third party. The documentation supporting a European marketing authorisation is publicly available on the European Medicines Agency (EMA) website, and this enables a patentee to apply for an SPC for a product protected by its patent without recourse to the owner of the marketing authorisation. Had Lilly obtained a marketing authorisation before the October 2016 patent expiry, HGS could have used the documents on the EMA website to obtain an SPC and used that SPC to seek to prevent Lilly marketing tabalumab for a further five year period.

Lilly's position was that HGS should not be rewarded with an SPC for Lilly's extensive investment in progressing from the disclosure in the '804 patent of "neutrokine-α and its antibodies with a practical use for these purposes yet to be discovered" to identifying tabalumab and taking it through clinical trials. Lilly therefore applied to the English High Court for a declaration that any SPC that may be sought in respect of HGS's '804 patent which relies on the MA for Lilly's tabalumab antibody would be invalid by reason of Article 3(a) of the SPC regulation by reason of the fact that nowhere was tabalumab specified or identified in the wording of the '804 Patent (referred to as 'the Specification issue'). Lilly also argued that HGS should not be able to file for an SPC based on a competitor's MA (referred to as 'the Third Party Issue', see below), but dropped this aspect having failed to secure a timely reference to the CJEU on this point.

Article 3 of the SPC regulation (469/2009) reads:

A certificate shall be granted if, in the Member State in which the application referred to in Article 7 is submitted and at the date of that application:

1. the product is protected by a basic patent in force;
2. a valid authorisation to place the product on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC or Directive 2001/82/EC, as appropriate;
3. the product has not already been the subject of a certificate;
4. the authorisation referred to in point (b) is the first authorisation to place the product on the market as a medicinal product.

"Protected by a basic patent"

Article 3(a) has been the subject of many cases. What does 'protected by a basic patent' mean? A number of cases have concerned combination products and are of limited relevance but three main principles emerge. First, "the protection conferred by the certificate cannot exceed the scope of protection conferred by the basic patent" (Farmitalia[5]). Second, "it follows that Article 3(a) of the regulation precludes the grant of a SPC relating to active ingredients which are not specified in the wording of the claims of the basic patent." (Medeva[6]). Third, "the test laid down by the Court of Justice in Medeva and its progeny is unclear save in its rejection of the infringement test in combination cases" (Novartis v Medimmune[7]).

However, this leaves a number of questions, as articulated by Arnold J in Novartis v Medimmune: "In particular, it is unclear precisely what is meant by "specified (or

identified) in the wording of the claims". Does this mean that it is sufficient for the product to fall within the scope of the claim on its true construction, or is something more required and if so what? For example, is it sufficient, say, for the claim to incorporate a Markush formula which covers a large number of compounds one of which is the product in respect of which an SPC is sought? Is it sufficient for the product to be defined in functional terms?"

How "specified" must something be to be "protected"? Both are imprecise words, and the Chancellor recognised as much in Medeva (Court of Appeal[8]), commenting that "the ambit of "specified" may range from express naming, through description, necessary implication to reasonable interpretation."

Warren J referred three questions to the CJEU to assist him in deciding the Lilly v HGS SPC case:

1. What are the criteria for deciding whether "the product is protected by a basic patent in force" in Article 3(a) of Regulation [No 469/2009]?
2. Are the criteria different where the product is not a combination product, and if so, what are the criteria?
3. In the case of a claim to an antibody or a class of antibodies, is it sufficient that the antibody or antibodies are defined in terms of their binding characteristics to a target protein, or is it necessary to provide a structural definition for the antibody or antibodies, and if so, how much?
4. The CJEU answered them in the round[9], saying:

"Article 3(a) ... must be interpreted as meaning that, in order for an active ingredient to be regarded as 'protected by a basic patent in force' within the meaning of that provision,

1. it is not necessary for the active ingredient to be identified in the claims of the patent by a structural formula.
2. where the active ingredient is covered by a functional formula in the claims of a patent... art 3(a) does not preclude... the grant of an SPC for that active ingredient on condition that **it is possible to reach the conclusion on the basis of those claims**, interpreted inter alia in the light of the description of the invention, as required by Article 69 of the Convention and the Protocol in the interpretation of that provision, that **the claims relate, implicitly but necessarily and specifically** , to the active ingredient in question, which is matter to be determined by the referring court."
3. (my paragraphs, omissions and underlining)

For those readers with a sketchy memory, Article 69 EPC reads "The extent of the protection conferred by a European patent or a European patent application shall be determined by the claims. Nevertheless, the description and drawings shall be used to interpret the claims."

One thing is clear: a functional claim does not preclude an SPC. The second clear point is that an SPC can be granted if the claims "relate, implicitly but necessarily and specifically" to the active ingredient in question. But what does that mean? Do the words 'implicitly', 'necessarily' and 'specifically' add something to 'relate'? What does 'relate' mean? If it were a simple infringement test then would the extra words be needed? Warren J (para 70) held[10] that "the correct reading of [39] of the Judgment and the answer the Court gives, demand an application of the relevant rules (Article 69 or section 125) to ascertain the extent of the invention and what the claims relate to. If the active ingredient in question is covered by the claims, the active ingredient is, subject to the proviso explained at paragraph 66 above, protected for the purposes of Article 3(a)."

The proviso at paragraph 66 relates to products which are combinations of active ingredients, so what Warren J appears to be saying is that the test is in effect an infringement test except in combination cases. Would Warren J's test give the same answer as the CJEU on the facts of Actavis v Sanofi?[11] The patent in that case claimed irbesartan and a diuretic (with no use of the word 'comprises') and it could be argued that the combination of irbesartan and hydrochlorothiazide was no less "covered by the claims" than tabalumab was, and therefore "protected for the purposes of Article 3(a)."

Turning away from the patent and to the SPC, Warren J (para 18) explains that an SPC is not to confer more extensive rights than the basic patent. What rights does an SPC confer? Article 4 provides that "...the protection conferred by a certificate shall extend only to the product covered by the authorisation to place the corresponding medicinal product on the market..." That is to say that the SPC confers the right to prevent others selling, in this case, tabalumab. It was common ground between the parties, and restated by the CJEU at paragraph 36 of its judgment, that "tabalumab was not specified in the '804 patent" in the sense that it was not expressly named nor was it possible to find a description of it in the patent. The '804 patent, recall, disclosed neutrokine-α and antibodies thereto, but had a "practical use yet to be discovered". Between the disclosure of the '804 patent and tabalumab was a development program to work out what neutrokine-α does, how that activity might be assayed, how that function translates into diseases, how those diseases might be treated, generating an antibody which might be useful, testing in vitro and in vivo in animals, formulating and trialling that antibody in human clinical trials. In effect this means that the SPC would be granting slightly different rights to

the '804 patent. It would be granting the rights to the fruit of many years of extra work over and above that disclosed in the patent.

So, how 'specified' should a product be to qualify as 'protected'? Warren J comments on the two ends of the spectrum of definitions of 'specified'.

The patent at the non-specific end of the spectrum does not name nor describe the product. Warren J quotes and agrees with counsel for HGS as saying "it would be illogical to conclude that fundamental research which merited the grant of a patent and opened up the field, enabling the production of all specific antibodies to a new target protein did not merit supplementary protection because it was somehow too fundamental to count" (para 53). So, any patent no matter how non-specific can qualify as a 'basic patent'. This is supported by Advocate General Fennelly's comment in Case-181/95 (Biogen), "Article 1(c) of the Regulation suggests that any patent, including one based on the most elementary research, may be designated as a basic patent...".

The patent at the specific end of the spectrum names a product, but Warren J felt[12] that "... it cannot be that the Court is requiring an individualised description of the particular active ingredient...".
Warren J considers whether there might be some middle ground but dismisses it, commenting "But if something less is sufficient, what is it? There is no firm foundation for adopting any particular definition as sufficient and, certainly, the Court gives no guidance at all about that." This is unfortunate, because there is a large space on the spectrum of definitions of 'specified' between the disclosure of neutrokine-α and the disclosure of a particular active ingredient antibody. For example, a patent could claim antibodies to a particular epitope, with data showing that epitope to be important in a particular disease and examples of some promising example antibodies encompassed by the functional claim definition.

The CJEU, in its answers to Warren J's questions, did discuss the spirit of the SPC regulation, which might shed some light on how far along the spectrum the patent must specify, but this was thought by Warren J to be relevant to the Third Party Issue rather than the case in hand. The CJEU quoted Recitals 4, 5, 9 and 10 in the preamble to the regulation:

4. At the moment, the period that elapses between the filing of an application for a patent for a new medicinal product and authorisation to place the medicinal product on the market makes the period of effective protection under the patent insufficient to cover the investment put into the research.

5. This situation leads to a lack of protection which penalises pharmaceutical research.

9. The duration of the protection granted by the certificate should be such as to provide adequate effective protection. For this purpose, the holder of both a patent and a certificate should be able to enjoy an overall maximum of 15 years of exclusivity from the time the medicinal product in question first obtains authorisation to be placed on the market in the Community.
10. All the interests at stake, including those of public health, in a sector as complex and sensitive as the pharmaceutical sector, should nevertheless be taken into account. For this purpose, the certificate cannot be granted for a period exceeding five years. The protection granted should furthermore be strictly confined to the product which obtained authorisation to be placed on the market as a medicinal product.'

and then set out its comments in paragraphs 41, 42 and 43:

41. Moreover, it should be recalled that the SPC is designed simply to re-establish a sufficient period of effective protection of the basic patent by permitting the holder to enjoy an additional period of exclusivity on the expiry of that patent, which is intended to compensate, at least in part, for the delay to the commercial exploitation of his invention by reason of the time which has elapsed between the date on which the application for the patent was filed and the date on which the first MA in the European Union was granted (Case C-229/09 Hogan Lovells International [2010] ECR I-11335, paragraph 50; Case C-443/12 Actavis Group PTC and Actavis UK [2013] ECR, paragraph 31; and Case C-484/12 Georgetown University [2013] ECR, paragraph 36).
42. As stated in recital 4 in the preamble to Regulation No 469/2009, the purpose of that additional period of exclusivity is to encourage research and, to that end, it is designed to ensure that the investments put into such research are covered.
43. In the light of the objective of Regulation No 469/2009, the refusal of an SPC application for an active ingredient which is not specifically referred to by a patent issued by the EPO relied on in support of such an application may be justified - **in circumstances such as those in the main proceedings and as observed by Eli Lilly - where the holder of the patent in question has failed to take any steps to carry out more in-depth research and identify his invention specifically, making it possible to ascertain clearly the active ingredient which may be commercially exploited in a medicinal product corresponding to the needs of certain patients**. In such a situation, if an SPC were granted to the patent holder, even though - since he was not the holder of the MA granted for the medicinal product developed from the

specifications of the source patent - that patent holder had not made any investment in research relating to that aspect of his original invention, that would undermine the objective of Regulation No 469/2009, as referred to in recital 4 in the preamble thereto.

In summary, the refusal of an SPC application on the basis of lack of specification[13] may be justified where the holder of the patent has failed to carry out research and identify his invention and the active ingredient which may be commercially exploited. To grant an SPC in that situation would undermine the objective of the SPC regulation. Is the CJEU saying that the SPC rules undermine the objective of the SPC regulation, or is it saying that there might be a definition of 'specified' somewhere between Warren J's two extremes? Or is it (in the underlined section), rather indirectly, following on from its comments in paragraphs 34 ("...the regulation precludes the grant of an SPC relating to active ingredients which are not specified...") and 38 ("...an active ingredient which is not identified...cannot be considered to be protected...") and stating that in its opinion the holder of the patent did indeed fail to "identify his invention specifically"?

The lack of conformity between the objective of the regulation and the various proposed definitions of 'specified' must lead to a suggestion that whether a product is 'protected by a basic patent' must be determined by a sui generis construction. It is not an infringement test (paragraphs 33 and 37 CJEU) and it is not an individualised disclosure test, so what is it?

Hoffmann LJ, in Amgen[14], said that a patent should be construed to mean "what the notional addressee would have understood the author to mean by using those words". This, surely, is what the CJEU is driving at in its rather obtuse answers. Arnold J, in Actavis v Sanofi[15], explained that he felt that the active ingredient should embody "the inventive advance (or technical contribution) of the basic patent.", wording echoed by the CJEU when it explained that the purpose of the regulation is to "compensate for the delay to the marketing of what constitutes the core inventive advance that is the subject of the basic patent" in its answers in the same case[16]. Would the notional addressee understand the '804 patent to be about the discovery of neutrokine-α and its great potential or would he understand it to be about specific pharmaceutical antibodies ("a patent for a new medicinal product" per Recital 4)? Questions about structure and function, combination or not, are sideshows to the basic question of how to construe a patent for the purpose at hand.

There should be no need for an "an approach which discriminated between different stages of the research leading to an MA" nor any "detailed enquiry about the extent to which work done at an early stage had value in the research done at a later stage"

(Warren J [17]), only an approach which construes the patent correctly. This is more difficult than Warren J's test, and has no firm foundation for adopting any particular definition, but if the courts can navigate the seas of interpretative uncertainty in patent cases then they should be competent to deal with them in SPC cases.

Third Party Issue

Lilly dropped the Third Party argument in the court proceedings but it remains a live issue for industry. Is it right that SPC squatting is allowed? It is not uncommon in the biotech industry that different antibodies developed by different companies would infringe the same earlier 'functional antibody claiming patent': is it right that all those companies should be discouraged from investing in the clinical development of new medicines by a fear of the patentee engaging in SPC squatting? One can argue that those companies go into the situation with eyes open: no company developing a product to the point of obtaining marketing authorisation will be unaware of relevant patent protection and the consequent risk of SPC squatting, but what are the options? 1) take a licence, 2) delay application for marketing authorisation until the patent has expired, 3) apply to revoke the patent, 4) apply to invalidate the SPC.

Is option 1 realistic? Will a patentee willingly grant a licence on a product competing with its own, assuming it has also has a product on the market? Will a competing patentee grant a licence on reasonable terms even if it has no competing product?

Is option 2 the best outcome for patients and/or health authority budgets? Option 2 is a de facto extension of the term of the patent and delays the entry onto market of a drug potentially better and/or cheaper than the one already available, or for different indications.

Option 3 would only occur in a minority of cases. One would imagine that the third party had already attempted to revoke the patent in order to come onto the market earlier.

Option 4 is the path Lilly has taken (following a failed attempt to revoke the patent) but Warren J's ruling would seem to tilt the balance in favour of the patentee in this genre of case.

A system more attuned to the objective of the SPC regulation would permit the patentee to apply for the SPC only with the permission of the marketing authorisation holder. After all, the purpose of the SPC regulation is to compensate for the time between filing "an application for a patent for a new medicinal product and authorisation to place the

medicinal product on the market" (Recital 4), and an SPC in effect protects the extra investment made to take the product from invention to medicinal product. Why then does the person who did the work to obtain the marketing authorisation not have a say in the application for an SPC? By comparison, the equivalent system in the US, the patent term extension, requires that the patentee applicant must be able to provide evidence that a product has been diligently developed to approval and therefore must either be the person which performed the clinical development, or be on good terms with that person. This requirement crystallises the link between the investment made in clinical development and the extension of protection, which is missing in the SPC regulation. In connection with this, we understand that the CJEU asked the European Commission whether there was any intention to revise the SPC regulation, to which the reply was "the mind is willing but the flesh is weak."

Footnotes

[1] Page 24, line 18 of the transcript of Eli Lilly v Human Genome Sciences, 18 July 2014
[2] [2012] EWCA Civ 1185
[3] [2012] EWCA Civ 1185
[4] See Arnold J. in Novartis Pharmaceuticals UK Limited v Medimmune Limited and or [2012] EWHC 181 para.61 under the heading: "A point not taken".
[5] C-392/97.
[6] C-322/10.
[7] [2012] EWHC 181
[8] [2013] EWCA Civ 523
[9] C-493/12
[10] [2014] EWHC 2404 (Pat)
[11] [2012] EWHC 2545 and C-442/12
[12] Para 74 [2014] EWHC 2404 (Pat)
[13] The CJEU was aware that the Third Party issue had been dropped from the case.
[14] [2004] UKHL 46
[15] [2012] EWHC 2545 (Pat) paragraph 76
[16] C-443/12 paragraph 41
[17] Para 47 [2014] EWHC 2404 (Pat)