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NO CLEAR POINTER IN THE RIGHT DIRECTION: VALIDITY ISSUES IN EUROPE OF PATENT TERM EXTENSIONS COVERING FIXED-COMBINATION MEDICINAL PRODUCTS

Pitfalls loom when applying for patent term extensions covering fixed combination medicinal products. Attention has to be paid during prosecution to the impact of the wording of claims on availability of patent term extensions for combination products. At the same time, those involved in product development should take into account the wording of the claims with a view toward securing patent term extension.

This *Commentary* addresses the validity of European patent term extensions, namely supplementary protection certificates ("SPCs"), covering fixed-combination medicinal products.

An SPC provides an extension of the patent term by a maximum of five years in order to compensate patent proprietors for the time consumed by development and the market authorization procedure required for medicinal and plant protection products.

SPCs for medicinal products are granted on the basis of the European Community Regulation 469/2009 concerning the supplementary protection certificate for medicinal products ("SPC Regulation").

Article 3 of the SPC Regulation stipulates four basic requirements for obtaining a certificate, the first two being of particular relevance for the validity of SPCs covering fixed-combination medicinal products. Art. 3 (a) requires that the product—the active pharmaceutical ingredient ("API") or a combination of APIs—be protected by a basic patent in force, and Art. 3 (b) requires that a valid authorization to place the product on the market as a medicinal product ("marketing authorization") must have been granted.

The question arises whether the requirements of Art. 3 (a) and (b) are fulfilled when the patent claims the API A, but the SPC application is relying on the authorization for a medicinal product containing API A in combination with a further API B. The same question arises when the basic patent claims a combination of two APIs, A and B, whereas the SPC application refers only to API A. Similarly, the SPC application may refer

to API(s) that are not identical to those used in the authorized medicinal product.

Although the SPC Regulation is based on European Community law, and the Court of Justice of the European Union (Court of Justice, CJ) is the final authority to decide about legal issues relating to SPCs, national authorities such as patent offices are appointed to grant SPCs. Also, appeals from the rejection of SPCs are dealt with by national courts. Thus, there has been a number of important decisions of national courts, in particular the High Court in London, relating to SPCs for fixed-combination medicinal products.

ART. 3 (A) OF THE SPC REGULATION

Regarding the requirement of Art. 3 (a) of the SPC Regulation, it appears that there are two different concepts of how to handle the question of whether the product, *i.e.*, the API, is protected by the basic patent. Some of the national jurisdictions seem to follow the so-called "infringement test," and other jurisdictions appear to apply a test that can be described as the "identification test."

The rationale behind the "infringement test" appears familiar: whether a fixed-combination medicinal product containing the APIs A and B, which is the object of an SPC application, would infringe a patent claiming the API A. Applying the basic principles of infringement, it would seem that the product of the SPC infringes the patent because the combination of A and B fulfills all features of a claim directed to A. Thus, in such a situation, the product of the SPC is regarded as being protected by the basic patent pursuant to Art. 3 (a) of the SPC Regulation. In contrast, an SPC referring to an API A only would not infringe a patent claiming the combination of A and B and would thus not be in accordance with Art. 3 (a). This position appears to be taken for instance by the German Federal Court of Justice (see below for details).

In contrast, in other jurisdictions, it is held that the application of the principles of infringement confers the patent proprietor a legal position far beyond what was intended by the SPC Regulation. Instead, the product that is the object of the certificate must be identifiable with the invention of the designated basic patent.

This kind of "identification test" was applied in various decisions of the High Court of London (cf. *Takeda*, 2003 EWHC 649 (Pat), *Gilead*, 2008, EWHC 1902 (Pat); *Astellas*, 2009, EWHC, 1916 (Pat); *Medeva*, 2010, EWHC, 68 (Pat)) and the U.K. Patent Office (*Imclone – Aventis*, 2010, O/066/10). Also, the Dutch and Swedish authorities appear to follow this concept (*Ranbaxy v. Warner-Lambert*, 2008, The Hague Court of Appeal, IEPT20080221; *Aventis*, 2009, District Court of the Hague/Council of State, JGR 2008/32; *A/B Hässle*, Supreme Administrative Court of Sweden, Case number 3248-1996). However, the question of how clearly identifiable in the basic patent the object of the certificate must be remains uncertain.

In the *Gilead* case, the basic patent covered a class of new antiretroviral compounds useful in the treatment of HIV, including tenofovir. Gilead Sciences, Inc. sought SPC protection for a combination of tenofovir and another antiretroviral called emtricitabine. The hearing officer did not consider the combination of tenofovir and emtricitabine to be protected by a claim directed to tenofovir and argued that he could not find a "clear pointer" to the specific combination of antiretroviral compounds. In his opinion, the particular ingredient must be specifically disclosed.

On appeal, the High Court agreed with the hearing officer's opinion that a claim directed to compound A does not protect the combination of A and B in the sense of Art. 3 (a) of the SPC Regulation. However, the SPC was granted on the basis of a dependent claim directed to a combination of tenofovir and "other therapeutic ingredients." The High Court did not agree that a "clear pointer" was required and considered this test—which is not set out in the SPC Regulation—to be too vague. According to the High Court, the test as set out in *Takeda* was to identify the active ingredients of the product that are relevant to a consideration of whether the product falls within the scope of a claim of the basic patent. It is those ingredients, and only those ingredients, that can be said to be protected within the meaning of the SPC Regulation. The High Court considered that the combination of

tenofovir and emtricitabine fell within the scope of the claim of the basic patent.

Thus, the "identification test" applied in the *Gilead* case did not require the specific disclosure in the basic patent's claims of the combination of API referred to in the SPC application. At the same time, it was admitted that compared to the "infringement test," the application of the "identification test" could produce harsh results.

How harsh these results can be becomes apparent from another case decided by the High Court (*Medeva*, 2010, EWHC, 68 (Pat)). In the *Medeva* case, five different applications for SPCs for a variety of combination vaccines were at issue. The underlying basic patent claimed vaccines against whooping cough containing the antigens pertactin and filamentous haemagglutinin ("FHA"). In fact, all five SPC applications referred to API combinations of pertactin and FHA, but four of them additionally contained numerous other antigens for vaccination against various diseases. Only one of the SPC applications was for pertactin and FHA only.

The High Court denied the SPCs covering pertactin and FHA together with other antigens because the other antigens were considered as not being identifiable in the basic patent. Thus, although national health policies in some instances force companies to market combination vaccines directed to multiple diseases and to apply for marketing authorizations covering these combination vaccines, the SPCs were denied. The High Court acknowledged that this harsh result is produced by the application of the "identification test," but these results are not limited to the field of vaccines, and there is no basis in the SPC Regulation for applying different criteria to different classes of products.

The Court of Appeal recently referred this case to the Court of Justice for a preliminary ruling on several questions regarding Art. 3 (a) and (b) of the SPC Regulation. In particular, the Court of Appeal queries the test to be applied in order to determine whether "the product is protected by a basic patent in force." Moreover, with reference to the particular situation in the *Medeva* case, the Court asked whether a different test should be applied in cases where the product is a multi-disease vaccine and whether it is sufficient for the purpose of Art. 3 (a), in the context of a multi-disease vaccine, that the basic patent in force protects one aspect of the product. Similarly, with regard to Art. 3 (b), the Court asked if the product may be limited to the part of a multi-disease vaccine that is protected by the basic patent in force.

Pending a decision of the Court of Justice, the application of the "identification test" results in a reduced freedom of the patent proprietor to choose the form in which a new pharmaceutical is to be placed on the market. Accordingly, the holder of a patent claiming API A is restricted to a medicinal product containing A and cannot market a fixed-combination medicinal product containing A and B in case supplementary protection by an SPC is desired.

As discussed above, the introduction of an "identifier" toward the combination of APIs into the claims of the patent, *e.g.*, a claim directed to an API in combination with at least "other therapeutic ingredients," could overcome these limitations. However, careful attention should be paid to make this a dependent claim only and not to limit the claims to fixed-combinations only (to the extent possible with regard to novelty and inventive step). Inadvertently limiting the claims to fixed-combinations only would result in significantly raising the regulatory bar for successful application for a marketing authorization. Applications for fixed-combination products may not only refer to the respective ingredients and dossiers thereto, but have to provide a dossier on the fixed-combination as such, justifying the use of the fixed-combination over the use of the respective single compound products.

ART. 3 (B) OF THE SPC REGULATION

Whether an "identifier" in the right direction could also overcome rejections based on the requirement of Art. 3 (b) of the SPC Regulation is questionable because of the difference between the underlying legal provisions, *i.e.*, the difference between Art. 3 (a) and Art. 3 (b).

In the above-mentioned U.K. cases *Imclone – Aventis* and *Medeva*, an SPC was denied because the API of the SPC application did not correspond to the respective marketing authorization. In the *Takeda* case, refusal was based on Art. 3 (a), but Art. 3 (b) was also discussed in the reasons.

As mentioned above, in the *Medeva* case, one of the five SPC applications was for pertactin and FHA only. However, all five marketing authorizations were for vaccines containing pertactin and FHA in combination with numerous other antigens for vaccination against various diseases. In the *Imclone – Aventis* and *Takeda* cases, in summary, the SPC application was for the combination of A and B, but the relevant marketing authorization only covered A. In all three cases, it was considered that the requirement of Art. 3 (b) of the SPC Regulation had not been fulfilled.

Interestingly, in the *Takeda* case, the High Court argued that even if a marketing authorization contains information implying that the product may (or should) be used as a combination therapy, the marketing authorization is for the single product and not for a combination therapy. Hence, such "identifier" contained in the marketing authorization was not considered to establish compliance with Art. 3 (b) of the SPC Regulation.

Also, in a similar situation, the German Federal Court of Justice ("BGH") was presented with a case where the SPC application related to a combination of pantoprazol and certain anti-helicobacter compounds (*Anti-Helicobacter Präparat*, BGH - X ZB 1/08). The marketing authorization was obtained for a medicinal product containing only pantoprazol. The basic patent claimed the combination of pantoprazol and the anti-helicobacter compounds. Although the marketing authorization contained an "identifier" in the right direction (in that it referred to the possible use of pantoprazol for certain types of cancer in combination with the respective anti-helicobacter compounds), the BGH denied the grant of an SPC. Interestingly, in its reasoning, the BGH did not focus on the question of whether the product of the SPC is covered by the marketing authorization, but discussed the scope of protection of the basic patent. The BGH considered that a basic patent claiming a combination of A and B does not confer protection for A or B alone. Thus, although dealing with Art. 3 (b) of the SPC Regulation, the BGH considered the scope of protection of the basic patent in order to reject the SPC application. However, also in this case, the "identifier" in the marketing authorization did not remedy the discrepancy between the products of the SPC and the marketing authorization.

Regarding the above decision, it is further interesting to note that the BGH also stated that the protection conferred by the SPC must fall within the scope of the basic patent. As already discussed above, this indicates that with regard to Art. 3 (a) of the SPC Regulation, the BGH appears to apply the "infringement test" rather than the "identification test."

THE TAKE-AWAY

Several decisions from national courts, in particular the High Court of London, confirm that applicants for SPCs for combination products can be caught between the requirements of Article 3 (a) and Article 3 (b) of the SPC Regulation. Although this *Commentary* focuses on SPCs for medicinal products, consequences outlined herein will be equally applicable to SPCs for plant protection products.

With regard to Art. 3 (b), the ruling of national authorities appears to be consistently restrictive and in line with several decisions of the Court of Justice instructing to interpret the term "product" in Art. 3 (b) narrowly (*Massachusetts Institute of Technology*, 2006, CJ, C-431/04; *Yissum*, 2007, CJ, C392/97).

Concerning Art. 3 (a), there appears to be no uniform way to interpret this provision in the different EC member states. Although the Court of Justice ruled that the criteria for the application of Art. 3 (a) are determined by the national law relevant for the basic patent (*Farmitalia*, 1999, CJ, C-392/97), *i.e.*, Art. 69 of the European patent convention and its protocol in conjunction with the national case law regarding the scope of protection, it is not clear whether the Court of Justice either endorses or rejects the "infringement test."

While waiting for the Court of Justice to decide on the *Medeva* case, the *Gilead* case teaches that even when applying the stricter "identification test," one can be saved by including in the basic patent a claim for the active ingredient in combination with at least "other therapeutic ingredients," preferably in combination with specific candidates for future combination therapy. This should be kept in mind when drafting patent specifications and claims.

But even without an "identifier" that could prevent refusal of an SPC application in a country applying an "identification test," filing an SPC application covering a combination product in countries applying the "infringement test" might be worthwhile to consider. Protection in a few major European countries might be sufficient to prevent competitors from starting production, because entering the market with a pharmaceutical product only in some European countries might not be viable from a business perspective.

For pending proceedings, where the circumstances are as described above, a request for suspension of the proceedings until the Court of Justice has decided in the *Medeva* case should be considered. This might be advantageous not only in cases where SPC applications are refused by granting authorities but also in national invalidation proceedings where a granted SPC is attacked as not fulfilling the requirements of Art. 3 (a) and 3 (b) of the SPC Regulation.

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