

## Newsletter January 2014 for Health & Life Science Industry

### Legal Practice in the EU

#### Plenty of SPC Action at the End of the Year

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On 14 November 2013, the CJEU issued two so-called reasoned orders and on 12 December 2013 – the Super SPC Thursday – three long-awaited judgments.

In this article, we would like to provide you with a brief overview of these newly decided cases:

[C-210/13 GlaxoSmithKline v Comptroller-General of Patents](#)

[C-617/12 AstraZeneca AB v Comptroller-General of Patents](#)

[C-443/12 Actavis v Sanofi](#)

[C-493/12 Eli Lilly v HGS](#)

[C-484/12 Georgetown University v OCN](#)

#### **C-210/13 GlaxoSmithKline v Comptroller-General of Patents**

##### **Background**

In our previous [Newsletter of July 2013](#), we discussed the referral of C-210/13 to the CJEU.

##### **Questions**

The questions referred to the CJEU were the following:

1. *Is an adjuvant which has no therapeutic effect on its own, but which enhances the therapeutic effect of an antigen when combined with that antigen in a vaccine, an "active ingredient" within the meaning of Article 1(b) of the SPC-Regulation?*
2. *If the answer to question 1 is no, can the combination of such an adjuvant with an antigen nevertheless be regarded as a "combination of active ingredients" within the meaning of Article 1(b) of the SPC-Regulation?*

##### **Ruling**

The answer given in the reasoned order reads as follows: "Article 1(b) [...] must be interpreted as meaning that, just as an adjuvant does not fall within the definition of "active ingredient" within the meaning of that provision, so a combination of two substances, namely an active ingredient having therapeutic effects on its

*own, and an adjuvant which, while enhancing those therapeutic effects, has no therapeutic effect on its own, does not fall within the definition of "combination of active ingredients" within the meaning of that provision".*

In order to avoid legal uncertainty with regard to the application of the SPC-Regulation, the CJEU held that the term "product" should be interpreted narrowly, as held in [C-431/04](#), to the effect that the term "product" cannot cover a substance which does not correspond to the definition of "active ingredient" or that of "combination of active ingredients".

### **C-617/12 AstraZeneca AB v Comptroller-General of Patents**

#### **Background**

AstraZeneca is the proprietor of a European patent ("EP") covering the active ingredient gefitinib, which is due to expire on 22 April 2016.

In July 2002, AstraZeneca applied for an authorisation with Swissmedic to place the medicinal product Iressa on the market in Switzerland. With that application, AstraZeneca submitted clinical data from two Phase II studies. Swissmedic granted the requested authorisation under a fast-track procedure on 2 March 2004 ("the Swiss MA"). That MA was, however, conditional on the provision of further clinical data to demonstrate the effects of Iressa.

Due to the customs union between Switzerland and Liechtenstein, relating, inter alia, to patents, the Swiss MA was automatically recognised in Liechtenstein. The referring court pointed out in that regard that there was, however, no direct evidence that Iressa was actually sold in Liechtenstein during the ensuing period.

Swissmedic suspended that Swiss MA on 24 October 2005, with the result that, from that date, it was no longer possible to distribute Iressa in Switzerland or Liechtenstein, except to supply that medicinal product to individual patients, which had to be specifically approved by Swissmedic.

In January 2003, AstraZeneca submitted an application to the EMA for an MA for Iressa under Council Regulation (EEC) No 2309/93. The new Committee for Medicinal Products for Human Use ("CHMP") refused to grant an MA on the basis of the Phase II studies for Iressa provided by AstraZeneca. Moreover, the data generated by the Phase III studies submitted by AstraZeneca did not enable it to provide satisfactory answers to the questions raised by the CHMP and, therefore, AstraZeneca withdrew its MA application in January 2005.

In May 2008, AstraZeneca resubmitted its application to the EMA with a refined therapeutic indication, which was supported by further studies undertaken so as to address the CHMP's concerns with the original application. On the basis of said data, the EMA granted an MA for Iressa on 24 June 2009 ("the European MA").

In June 2008, AstraZeneca requested that Swissmedic lift the suspension of the Swiss MA and amend the indications for Iressa, submitting further studies in that regard. Swissmedic lifted the suspension on 8 December 2010.

On 11 December 2009, AstraZeneca applied for an SPC with the Patent Office for the active ingredient gefitinib, on the basis of its EP and the European MA.

The Patent Office granted the SPC on 2 April 2012. However, with regard to the duration of the SPC, calculated according to Art. 13(1) of the SPC-Regulation, the Patent Office considered that the Swiss MA was to be regarded as the first MA for the purpose of that provision. AstraZeneca challenged the Patent Office's decision.

## Questions

The questions referred to the CJEU were the following:

1. *Is a Swiss MA not granted pursuant to the administrative authorisation procedure laid down in Directive 2001/83, but automatically recognised by Liechtenstein, capable of constituting the "first authorisation to place the product on the market" for the purposes of Article 13(1) of the SPC-Regulation?*
2. *Does it make a difference to the answer to the first question if:*
  - a. *the set of clinical data upon which the Swiss authority granted the MA was considered by EMA as not satisfying the conditions for the grant of a MA pursuant to Regulation No 726/2004; and/or*
  - b. *the Swiss MA was suspended after grant and was reinstated only following the submission of additional data?*
3. *If Article 13(1) of the SPC-Regulation refers solely to MAs granted pursuant to the administrative procedure laid down in Directive 2001/83, does the fact that a medicinal product was first placed on the market within the European Economic Area (EEA) pursuant to a Swiss MA automatically recognised in Liechtenstein, which was not granted pursuant to Directive 2001/83, render that product ineligible for the grant of an SPC, pursuant to Article 2 of the SPC-Regulation?*

In view of the answers given to Questions 1 and 2, there was no need to answer Question 3 according to the CJEU.

## Ruling

The answer given by the CJEU is as follows: *"In the context of the EEA, Article 13(1) of the SPC-Regulation must be interpreted as meaning that an administrative authorisation issued for a medicinal product by SwissMedic, which is automatically recognised in Liechtenstein, must be regarded as the first authorisation to place that medicinal product on the market within the meaning of that provision in the EEA where that authorisation predates MAs issued for the same medicinal product, either by the EMA, or by the competent authorities of European Union Member States in accordance with the requirements laid down in Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, and with the requirements of the Republic of Iceland and the Kingdom of Norway. The fact that, on the basis of similar clinical data, the EMA, unlike the Swiss authority, refused to grant a MA for that medicinal product at the conclusion of its examination of those data, or the fact that the Swiss authorisation to place the product on the market was suspended by the Swiss Institute for Medicinal Products and subsequently reinstated by the latter only when the holder of the authorisation submitted additional data to it are irrelevant."*

## **C-443/12 Actavis v Sanofi**

### **Background**

Sanofi is the proprietor of EP No. 0454511 covering a family of compounds which included the antihypertensive active ingredient irbesartan. The description also referred to pharmaceutical compositions containing a combination of active ingredients, one of which was a compound in accordance with the invention, whereas the other ingredient or ingredients could be a beta-blocking compound, a calcium antagonist, a diuretic, a non-steroidal anti-inflammatory or a tranquiliser.

Claims 1 to 7 of the basic patent were based on irbesartan alone, or on one of its salts. Claim 20 of the patent related to a pharmaceutical composition containing irbesartan associated with a diuretic. However, a specific diuretic was named neither in claim 20 nor in the description of the basic patent. That patent, granted on 17 June 1998, expired on 20 March 2011.

On the basis of that basic patent and MAs granted on 27 August 1997 for the medicinal product Aprovel, which had irbesartan as its single active ingredient and was used principally to treat primary hypertension, Sanofi obtained its first SPC for that active ingredient on 8 February 1999. That SPC expired on 14 August 2012. Also, based on the same basic patent but with MAs granted on 15 October 1998 for the medicinal product CoAprovel, comprising a combination of irbesartan and a diuretic (hydrochlorothiazide, used to treat primary hypertension), Sanofi obtained a second SPC for the combination of irbesartan and hydrochlorothiazide. That SPC was granted on 21 December 1999 and expired on 14 October 2013.

According to the summary of the European Public Assessment Report of the EMA, the combination of the two active ingredients had an additive effect, reducing the blood pressure more than either medicine alone. Therefore, curative properties of the combination of the two active ingredients corresponded to the total therapeutic effect which would otherwise be obtained by separate administration of Aprovel and hydrochlorothiazide. The summary states that the studies of Aprovel used with hydrochlorothiazide as separate tablets were used to support the use of CoAprovel, so that the combination had no new therapeutic effect when compared with the effects obtained when using those two active ingredients separately.

Actavis intended to market generic versions of both Aprovel and CoAprovel. However, since a generic medicinal product corresponding to CoAprovel would infringe Sanofi's second SPC for the combination of irbesartan and hydrochlorothiazide, Actavis brought proceedings before the Patents Court, England and Wales, challenging its validity.

### **Questions**

The questions referred to the CJEU were the following:

1. *What are the criteria for deciding whether "the product is protected by a basic patent in force" in Article 3(a) of the SPC-Regulation?*
2. *In a situation in which multiple products are protected by a basic patent in force, does the SPC-Regulation, and in particular Article 3(c), preclude the proprietor of the patent being issued a certificate for each of the products protected?*

## Ruling

The answer given by the CJEU reads as follows: *"In circumstances [...], where, on the basis of a patent protecting an innovative active ingredient and a MA for a medicinal product containing that ingredient as the single active ingredient, the holder of that patent has already obtained a supplementary protection certificate for that active ingredient entitling him to oppose the use of that active ingredient, either alone or in combination with other active ingredients, Article 3(c) of the SPC-Regulation must be interpreted as precluding that patent holder from obtaining – on the basis of that same patent but a subsequent MA for a different medicinal product containing that active ingredient in conjunction with another active ingredient which is not protected as such by the patent – a second supplementary protection certificate relating to that combination of active ingredients."*

On this basis, the CJEU held that in view of the answer given to Question 2, to the effect that a second SPC, such as that at issue in the main proceedings, may not be granted to Sanofi for the combination of irbesartan and hydrochlorothiazide, irrespective of whether that combination was protected as such by the basic patent within the meaning of Article 3(a) of the SPC-Regulation, there was no need to answer Question 1. The CJEU has, however, deliberated this issue in [C-493/12](#).

In its review of Question 2, the CJEU held 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 after the expiry of his patent, which is intended to compensate, at least in part, for the delay of 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.

The CJEU stated furthermore that in the main proceedings, Sanofi's patent, protecting the active ingredient irbesartan as such within the meaning of Article 3(a) of the SPC-Regulation, has already enabled its holder to obtain an SPC relating to that active ingredient. Moreover, it is common ground that hydrochlorothiazide, an active ingredient that is a member of a class of diuretics, is not protected as such by that patent or by any other patent. Additionally, the CJEU held that in accordance with Article 5 of the SPC-Regulation, an SPC granted in connection with a product confers, upon the expiry of the basic patent, the same rights as were conferred by that patent in relation to the product, within the limits of the protection conferred by the basic patent, as provided for in Article 4 of the SPC-Regulation. Accordingly, if, during the period in which the patent was valid, the patent holder could oppose, on the basis of his patent, the use or certain uses of his product in the form of a medicinal product consisting of such a product or containing it, the SPC granted in relation to that product would confer on the holder the same rights for all uses of the product, as a medicinal product, which were authorised before the expiry of that certificate. Thus, the CJEU held that in the main proceedings, since it is common ground that, during the period in which the first SPC was valid, Sanofi was entitled to oppose, on the basis of its basic patent, the use or certain uses of irbesartan in the form of a medicinal product consisting of such a product or containing it, the SPC (now expired) granted for that product also conferred on Sanofi the same rights for all uses of the product, as a medicinal product, which were authorised before the expiry of that certificate.

**C-493/12 Eli Lilly v Human Genome Sciences****Background**

Human Genome Sciences ("HGS") is the holder of EP No. 0 939 804, granted on 17 August 2005 and due to expire on 25 October 2016. The patent, relating to the discovery of a new protein, Neutrokin- $\alpha$ , disclosed and claimed that protein. It also related to antibodies that bind specifically to that protein. Neutrokin- $\alpha$  acts as an intercellular mediator in inflammation and immune response, which is why too much or too little of it may cause diseases of the immune system. Accordingly, antibodies that bind specifically to it may inhibit its activity and be useful in the treatment of autoimmune diseases.

Claims 13, 14 and 18 of that patent read as follows:

*"13. An isolated antibody or portion thereof that binds specifically to:*

- (a) the full length Neutrokin- $\alpha$  polypeptide (amino acid sequence of residues 1 to 285 of SEQ ID No: 2);*  
*or*
- (b) the extracellular domain of the Neutrokin- $\alpha$  polypeptide (amino acid sequence of residues 73 to 285 of SEQ ID No: 2).*

*14. The antibody or portion thereof of claim 13 which is selected from the group consisting of:*

- (c) a monoclonal antibody; [...]*

*18. A pharmaceutical composition comprising [...] the antibody or portion thereof of any one of claims 13 to 17 and, optionally, a pharmaceutically acceptable carrier."*

Eli Lilly wanted to market a pharmaceutical composition for the treatment of autoimmune diseases. That composition contains as its active ingredient the antibody LY2127399 (or "Tabalumab") which binds specifically to Neutrokin- $\alpha$ . However, Eli Lilly recognized that if it marketed that composition before the expiry of HGS's patent, LY2127399 would infringe claim 13 of said patent. The referring court therefore came to the conclusion that antibody LY2127399 is an antibody as defined in claim 13 of HGS's patent, namely an isolated antibody or portion thereof which binds specifically to Neutrokin- $\alpha$  polypeptide. Any pharmaceutical composition containing LY2127399 was thus a pharmaceutical composition falling under claim 18 of that patent.

Eli Lilly brought an action before the Patents Court, England and Wales, for a declaration that any SPC based on HGS' patent and on an MA for a medicinal product containing LY2127399 would be invalid, arguing that claim 13 of the basic patent was too broad for it to be possible for that antibody to be considered as being "specified" in that basic patent.

**Questions**

The questions referred to the CJEU were the following:

1. *What are the criteria for deciding whether "the product is protected by a basic patent in force" in Article 3(a) of SPC-Regulation?*

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?

## Ruling

The answer provided by the CJEU reads as follows: "Article 3(a) of SPC-Regulation 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, it is not necessary for the active ingredient to be identified in the claims of the patent by a structural formula. Where the active ingredient is covered by a functional formula in the claims of a patent issued by the European Patents Office, Article 3(a) of the SPC-Regulation does not, in principle, preclude the grant of a supplementary protection certificate 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 on the Grant of European Patents and the Protocol on the interpretation of that provision, that the claims relate, implicitly but necessarily and specifically, to the active ingredient in question, which is a matter to be determined by the referring court."

The CJEU commented that in recital 4 of the preamble to the SPC-Regulation, 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. In the light of the objective of the SPC-Regulation, 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 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. The CJEU held that 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 the SPC-Regulation, as referred to in recital 4 of the preamble thereto.

## C-484/12 Georgetown University v OCN

### Background

Georgetown's EP No. 0 647 140 claimed a vaccine for the prevention of papillomavirus infection, covering at least that protein, or fragment thereof, of, among others, HPV 16, HPV 18 or HPV 16 and HPV 18 together. The EP, granted on 12 December 2007, expired on 23 June 2013.

On 14 December 2007, Georgetown submitted eight SPC applications with the Dutch Patent Office ("OCN"), relying on the MA granted to Sanofi Pasteur on 20 September 2006 for the medicinal product Gardasil, which contains HPV-6, HPV-11, HPV-16 and HPV-18 purified proteins obtained from yeast cells, and on the MA granted to GlaxoSmithKline on 20 September 2007 for the medicinal product Cervarix, containing HPV-16 and HPV-18 purified proteins obtained from insect cells. Two of these applications concerned the combination of HPV-6, HPV-11, HPV-16 and HPV-18 and the combination of HPV-16 and HPV-18. Four other applications concerned SPCs with regard to, respectively, HPV-16, HPV-18, HPV-6 and HPV-11 individually. The two other applications also concerned HPV-16 individually and HPV-18 individually.

Whereas two SPC applications were granted, the SPC application based on the MA granted for Gardasil, which referred to the recombinant L1 protein of the human papillomavirus (HPV) type 16 as the "product" within the meaning of the SPC-Regulation, was rejected on 19 May 2010. The OCN argued that the MA related to a medicinal product containing additional active ingredients next to the recombinant protein of HPV-16. Georgetown University appealed the decision of the OCN.

## Questions

1. *Does the SPC-Regulation, more particularly Article 3(c) thereof, preclude, in a situation where there is a basic patent in force which protects several products, the holder of the basic patent from being granted a certificate for each of the protected products?*
2. *If the first question must be answered in the affirmative, how should Article 3(c) of the SPC-Regulation be interpreted in the situation where there is one basic patent in force which protects several products and where, at the date of the application for a certificate in respect of one of the products (A) protected by the basic patent, no certificates had yet been granted in respect of other products (B, C) protected by the same basic patent, but where certificates were nevertheless granted in respect of the products (B, C) before a decision was made with regard to the application for a certificate in respect of the first-mentioned product (A)?*
3. *Is it significant for the answer to the previous question whether the application in respect of one of the products (A) protected by the basic patent was submitted on the same date as the applications in respect of other products (B, C) protected by the same patent?*
4. *If the first question must be answered in the affirmative, may a certificate be granted for a product protected by a basic patent which is in force if a certificate has already been granted for another product protected by the same basic patent, but where the applicant surrenders the latter certificate with a view to obtaining a new certificate on the basis of the same basic patent?*
5. *If the issue of whether the surrender has retroactive effect is relevant for the purpose of answering the previous question, is the question of whether surrender has retroactive effect governed by Article 14(b) of the SPC-Regulation or by national law? If the question of whether surrender has retroactive effect is governed Article 14(b) of the SPC-Regulation, should that provision be interpreted to mean that surrender does have retroactive effect?*

In view of the answer given to Question 1, there was no need to answer Questions 2 to 5 according to the CJEU.

## Ruling

The answer provided by the CJEU reads as follows: *"In circumstances [...], where, on the basis of a basic patent and a MA for a medicinal product consisting of a combination of several active ingredients, the patent holder has already obtained a supplementary protection certificate for that combination of active ingredients, protected by that patent within the meaning of Article 3(a) of the SPC-Regulation, Article 3(c) of that regulation must be interpreted as not precluding the proprietor from also obtaining a supplementary protection certificate for one of those active ingredients which, individually, is also protected as such by that patent."*

The CJEU mentioned that the main proceedings concerned a situation in which the same basic patent could be regarded as protecting a number of products within the meaning of Article 3(a) of the SPC-Regulation, thus raising a different question, namely whether such a patent may permit its holder to obtain several SPCs. In that regard, it is possible, in principle, on the basis of a patent which protects several different "products",

to obtain several SPCs in relation to each of those different products, provided, inter alia, that each of those products is "protected" as such by that "basic patent" within the meaning of Article 3(a) of the SPC-Regulation, and is contained in a medicinal product with an MA. Accordingly, the CJEU stated that the wording of Article 1(b) and Article 3(c) of the SPC-Regulation does not preclude such an interpretation (however, see also C 443/12).

Furthermore, the CJEU observed that this interpretation was also consistent with the objective pursued by the SPC-Regulation, which, as is apparent from paragraph 11 of the Explanatory Memorandum, is to encourage research in the pharmaceutical sector by granting one SPC per product, a product being understood as an active substance in the strict sense. Any other interpretation might, moreover, give rise to circumvention tactics, entailing additional costs which may discourage innovation, in the sense that those concerned would be inclined to apply for a separate basic patent for each of their "products".