Case C-673/18

Request for a preliminary ruling

Date lodged:

30 October 2018

Referring court:

Cour d'appel de Paris (Court of Appeal, Paris, France)

Date of the decision to refer:

9 October 2018

Appellant:

SANTEN SAS

Defendant:

Directeur général de l'Institut national de la propriété industrielle

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[administrative references omitted]

COUR D'APPEL DE PARIS (COURT OF APPEAL, PARIS, FRANCE)

[administrative references omitted]

APPELLANT

SANTEN SAS

Simplified single shareholder company limited by shares, [...] [company registration number omitted] whose registered office is at

[company details omitted] 1000 EVRY

[name of company representative omitted]

[name of legal representative omitted]

THIRD PARTY:

DIRECTOR OF THE INSTITUT NATIONAL DE LA PROPRIÉTÉ INDUSTRIELLE (NATIONAL INSTITUTE FOR INDUSTRIAL PROPERTY, 'INPI')

[contact details of the institute omitted] 92677 COURBEVOIE CEDEX

[composition of referring court omitted]**[Or. 2]** [procedural details omitted]

JUDGMENT:

[procedural details omitted]

1 The Court of Appeal summarises the case as follows. SANTEN, a pharmaceutical laboratory specialising in ophthalmology, develops ophthalmic treatments for the three segments of the eye.

It holds European patent No EP 057959306 ('patent 306') filed on 10 October 2005 and granted on 31 December 2008 under the title 'Ophthalmic oil-in-water type emulsion with stable positive zeta potential', comprising 27 claims including the following:

R 1 An ophthalmic oil-in-water submicron type emulsion ...;

R 18 An ophthalmic emulsion according to any one of claims 1 to 17, comprising a pharmaceutically active substance;

R 20 An ophthalmic emulsion according to claim 18, wherein the active substance is an immunosuppressive agent selected in the group consisting of cyclosporine, sirolimus and tacrolimus;

R 21 An ophthalmic emulsion according to claim 20, wherein the active substance is cyclosporin A; **[Or. 3]**

R24 Use of an ophthalmic emulsion according to any one of claims 1 to 21, for the preparation of an ophthalmic composition for treating ocular conditions such as … keratitis ... .

The protection conferred by that patent expires on 11 October 2025.

On 19 March 2015, SANTEN obtained EU marketing authorisation ('MA') No EU/1/15/1990 [EU/1/15/990] for the medicinal product Ikervis. It is apparent from the summary of product characteristics that it is undisputed that the active ingredient of that medicinal product is ciclosporin [also spelled 'cyclosporine' and cyclosporin']. It has the form of an emulsion (eye drops) containing 1 mg of ciclosporin per ml. It is administered in a dose of one drop in the eye and treats severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes, consisting of inflammation of the cornea, the front part of the eye.

On 3 June 2015, on the basis of the patent and MA referred to above, SANTEN filed application No 15C0040 for a supplementary protection certificate (SPC) for a product called ‘ciclosporine collyre en émulsion’ [‘ciclosporin eye drops, emulsion’].

On 26 August 2015, in response to observations by the INPI, it renamed the product under the SPC ‘Ciclosporin for use in the treatment of keratitis’.

2 On 23 December 1983, a marketing authorisation had been granted for a medicinal product Sandimmun that already had ciclosporin as its active ingredient. That medicinal product was presented in the form of an oral solution containing 100 mg/ml of ciclosporin. It had several therapeutic indications, both in preventing the rejection of solid organ and bone marrow grafts and non-transplant indications including the treatment of endogenous uveitis, an inflammation of some or all of the uvea, the middle part of the eye.

3 By a decision of 6 October 2017, the director of the INPI rejected that application for an SPC.

4 By a declaration of 3 November 2017, SANTEN brought an action against that decision of the director of the INPI and on 1 December 2017 filed its first submissions.

By registered letters of 22 January 2018, SANTEN and the director of the INPI were called to attend the hearing of 19 June 2018.

5 In its most recent submissions, served on 17 May 2018, SANTEN applied to the Court of Appeal as follows:

Principal claims:

- To hold that the director of the INPI erred in rejecting SANTEN’s SPC application No 15C0040.

- To annul the decision of 6 October 2017 of the director of the INPI;

- To order the director of the INPI to grant SPC No 15C0040; **[Or. 4]**

In the alternative:

- To refer the following question to the Court of Justice of the European Union for a preliminary ruling:

‘Interpreting Article 3 of the SPC Regulation [Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products (codified version) (OJ 2009 L 152, p. 1], where a marketing authorisation (A) has been granted for a medicinal product containing an active ingredient, must Article 3(d) be interpreted

as precluding the grant of an SPC based on a later authorisation (B) for a different application of the same product where:

(i) the limits of the protection conferred by the basic patent extend not only to the second therapeutic application but also to a new formulation;

(ii) the earlier marketing authorisation was granted for a medicinal product for human use for a specific indication and the later marketing authorisation was also granted for a medicinal product for human use?'

- To stay proceedings pending the preliminary ruling by the Court of Justice

[...].

6 On 21 March 2018, the director of the INPI filed a pleading applying that the action be dismissed.

7 The case, in which oral arguments were submitted at the hearing on 19 June 2018, was adjourned [...] to the hearing of 3 July 2018 so that the director of the INPI and SANTEN could make submissions on the wording of any question to be referred for a preliminary ruling.

8 In his written pleadings served on 26 June 2018, the director of the INPI stated that he did not object to [the referral of questions] for a preliminary ruling, for which he proposed the following wording:

'1. Where the MA relied upon in support of an application for an SPC is not the first MA granted for the product, on the basis of what criteria can a "new therapeutic use" justifying grant of the SPC be established? In particular, in the light of the objectives of Regulation (EC) No 469/2009 of establishing a balanced system taking into account all the interests at stake, including those of public health, must the notion of a "new therapeutic use" be assessed according to stricter criteria than those for assessing the patentability of the invention?

2. Where an earlier marketing authorisation (A) has been granted for a medicinal product containing an active ingredient, must Article 3(d) be interpreted as precluding the grant of an SPC based on a later marketing authorisation (B) for a medicinal product using the same active ingredient but authorised for a different indication, where:

(i) the protection conferred by the basic patent covers a specific formulation of the active ingredient and is not used by the medicinal product to which the authorisation (A) relates;

(ii) the protection conferred by the basic patent is not limited to a specific therapeutic indication but covers the new formulation as such;
[Or. 5]

(iii) the later marketing authorisation (B) is limited to a therapeutic indication different from the therapeutic indications for which an earlier marketing authorisation (A) was granted;

(iv) the earlier marketing authorisation (A) was granted for a medicinal product for human use for a specific therapeutic indication and the marketing authorisation (B) was also granted for a medicinal product for human use?

(v) the basic patent relied upon in support of the application for an SPC protects use of the formulation to treat not only the disease referred to in the therapeutic indications in the MA relied upon in support of the application, but also to treat a disease referred to in the therapeutic indications of the earlier MA.'

9 On 29 June 2016, SANTEN served its submissions containing the following proposed wording of the question for a preliminary ruling:

'Where an earlier marketing authorisation (A) has been granted for a medicinal product containing an active ingredient, must Article 3(d) be interpreted as precluding the grant of an SPC based on a later marketing authorisation (B) for a medicinal product using the same active ingredient but authorised for a different indication, where:

(i) the protection conferred by the basic patent covers a specific formulation that is not the formulation used by the medicinal product to which the authorisation (A) relates, meaning that the SPC would not prevent exploitation of the previously authorised medicinal product;

(ii) the protection conferred by the basic patent is not limited to a specific therapeutic indication but covers the new formulation as such;

(iii) the later marketing authorisation (B) is limited to a therapeutic indication different from the therapeutic indications for which the earlier marketing authorisation (A) was granted;

(iv) the earlier marketing authorisation (A) was granted for a medicinal product for human use for a specific therapeutic indication and the marketing authorisation (B) was also granted for a medicinal product for human use?'

10 [...]. **[Or. 6]**

ACCORDINGLY

11 In order to reject SANTEN's application for a supplementary protection certificate for the medicinal product Ikervis the director of the INPI took the view that the marketing authorisation of 19 March 2015 was not the first marketing

authorisation, within the meaning of Article 3(d) of Regulation (EC) No 469/2009, for the active ingredient 'ciclosporin' in so far as a marketing authorisation had already been granted on 23 December 1983 for the medicinal product Sandimmun that also had ciclosporin as its active ingredient.

He added that the requirements in the Court of Justice's judgment of 19 July 2012 [*Neurim Pharmaceuticals (1991) Ltd* v *Comptroller-General of Patents*, (C-130/11, EU:C:2012:489)], on which SANTEN relies to argue that the medicinal product Ikervis included a new application of ciclosporin enabling a new SPC to be granted, seemed to him not to be satisfied since, first, the basic patent relied upon protected not only a new application of ciclosporin (claims 23 to 24) but also and primarily an ophthalmic oil-in-water submicron type emulsion containing an active substance, including ciclosporin (claims 1 to 21 and 25 to 26); furthermore and in any event, according to the director, it had not been shown that the medical application in the MA for the proprietary product Ikervis amounted to a new therapeutic application within the meaning of the *Neurim* case-law, compared with the proprietary product Sandimmun, since both concerned the treatment of inflammations in the field of ophthalmology.

In his pleading of 21 March 2018, he contends that the grant of an SPC, designed as an exceptional recompense for innovative medicinal products, requires several conditions to be satisfied. The Court of Justice, he submits, having interpreted restrictively the concept 'product', the active ingredient of a medicinal product, excluding considerations relating to its form, dosage, posology and therapeutic indications, in *Neurim* nuanced its case-law by allowing that, under certain circumstances, an MA, where it is not the first for the product, may nevertheless satisfy Article 3(d) if it is the first MA for a new medical use of the product falling within the limits of the protection conferred by the basic patent. According to the director, since that Court gave no indication of what the notion of a new therapeutic indication encompasses, it has been understood differently by the offices in the various EU Member States: the Netherlands office has confined the concept strictly to the situation in the *Neurim* case (an MA for human use as opposed to a veterinary MA) whereas the UK court has even wondered whether that concept should include new formulations of known products.

The French institution aims to take a measured approach in applying the *Neurim* case-law.

It is of the view, first, that the basic patent must have the same scope as the MA relied upon and, therefore, that scope must be limited to the new medical use corresponding to the therapeutic indication in that MA; that is the situation on the facts in *Neurim*; it is not the situation, it contends, in the present case, since the basic patent protects both a product, that is to say an ophthalmic emulsion in which the active substance is ciclosporin (claim 21), and the use of that emulsion to prepare an ophthalmic composition to treat numerous eye diseases that are referred to expressly, including not only keratitis but also, indeed, uveitis (claim 24). **[Or. 7]**

It asserts, secondly, that for it to be possible to grant an SPC, the MA relied upon must relate to an indication within a new therapeutic scope, in the sense of a new proprietary medical product, compared with the earlier MA, or a medicinal product in which the active ingredient acts differently from how it acts in the medicinal product to which the first MA relates. In the present case, in so far as both MAs were for the treatment of inflammation of parts of the human eye, using the same mechanism of action of ciclosporin, no new medicinal use has been sufficiently demonstrated.

12 SANTEN is seeking annulment of the decision of 6 October 2017 and, in the alternative, a [reference for a] preliminary ruling.

According to SANTEN, the application of the active substance ciclosporin is different, within the meaning of *Neurim*, in the Sandimmun and Ikervis proprietary medicines because:

- none of the earlier formulations of the proprietary medicine Sandimmun is the oil-in-water emulsion in claim no 1 of the basic patent relied upon for the Ikervis SPC;

- the Sandimmun and Ikervis proprietary medicines do not have the same therapeutic indication and treat different diseases; although in both instances ciclosporin has an anti-inflammatory function, amongst others, it is to treat different parts of the eye and different conditions;

- their posology and means of administration are different and the two proprietary medicines are not interchangeable.

SANTEN further asserts that the *Neurim* ruling does not contain any of the limitations that the director of the INPI is trying to include in it:

- the ruling is not confined to claims in the application but also covers basic patents protecting a new formulation;

- the principles it lays down are not confined to factual situations in which the first use was veterinary and the second human;

- it does not, according to SANTEN, require the basic patent to be limited to the new use.

13 According to Article 3, ‘Conditions for obtaining a certificate’, of Regulation (EC) No 469/2009 of 6 May 2009 concerning the supplementary protection certificate for medicinal products:

> ‘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:

(a) the product is protected by a basic patent in force;

(b) 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;

(c) the product has not already been the subject of a certificate;

(d) the authorisation referred to in (b) is the first authorisation to place the product on the market as a medicinal product.' **[Or. 8]**

The Court of Justice held as follows in its judgment of 19 July 2012, *Neurim* (C-130/11, EU:C:2012:489):

'Articles 3 and 4 of Regulation (EC) No 469/2009 of the European Parliament and of the Council of 6 May 2009 concerning the supplementary protection certificate for medicinal products must be interpreted as meaning that, in a case such as that in the main proceedings, the mere existence of an earlier marketing authorisation obtained for a veterinary medicinal product does not preclude the grant of a supplementary protection certificate for a different application of the same product for which a marketing authorisation has been granted, provided that the application is within the limits of the protection conferred by the basic patent relied upon for the purposes of the application for the supplementary protection certificate.'

14 In the present case, it is common ground that the application for supplementary protection certificate no 1 5C0040, for the product renamed 'ciclosporin for use in the treatment of keratitis', meets the requirements in Article 3(a), (b) and (c) above.

That product is protected by patent EP 306, which expires on 11 October 2025, in claims 1 (ophthalmic oil-in-water submicron type emulsion ...), 21 (... wherein the active substance is cyclosporin A ...) and 24 (… for the preparation of an ophthalmic composition for treating ocular conditions such as ... keratitis …) of that patent.

As the medicinal product known as Ikervis, it obtained Community marketing authorisation No EU/1/15/1990 on 19 March 2015.

It has not already been the subject of a supplementary protection certificate.

15 In contrast, it is also common ground that ciclosporin, the active ingredient of the medicinal product Ikervis, had already been the subject of a marketing authorisation, on 23 December 1983, as the medicinal product Sandimmun.

SANTEN nevertheless argues that this earlier authorisation does not preclude the grant of the SPC in question in so far as *Neurim* permits such a grant:

- for a different application of the same product;

- provided that application is within the limits of the protection conferred by the basic patent.

SANTEN and the director of the INPI disagree on the interpretation to be given to those concepts.

16 It is apparent from the evidence produced and the clarifications given that both medicinal products relate to the treatment of inflammation of parts of the eye in humans, using the same anti-inflammatory mechanism of ciclosporin.

However, they differ in their therapeutic indications and in factors relating to their formulation, dosage and posology. **[Or. 9]**

First of all, Sandimmun has several therapeutic indications, both in preventing the rejection of solid organ and bone marrow grafts and non-transplant indications including the treatment of endogenous uveitis, an inflammation of some or all of the uvea, the middle part of the eye. Ikervis can be used to treat severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes, consisting of inflammation of the cornea, the front part of the eye. It is not disputed that these are different diseases, affecting different parts of the eye.

Further, the proprietary medicine Sandimmun is presented as an oral solution containing 100 mg/ml of ciclosporin. To treat endogenous uveitis it is recommended that 5mg/kg/day be administered orally in 2 separate doses. The proprietary medicine Ikervis is in the form of an emulsion (eye drops) containing 1 mg of ciclosporin per ml. It is administered in a dose of one drop in the eye.

The director of the INPI argues that the concept of a different application within the meaning of *Neurim* should be interpreted strictly. Whilst not going so far as to claim that it should mean only the situation where an application for human use follows a veterinary application, the MA relied upon should relate to an indication falling within the new therapeutic scope, in the sense of a new proprietary medicine, compared with the earlier MA, or a medicinal product in which the active ingredient acts differently from how it acts in the medicinal product to which the first MA relates. In his draft question for a preliminary ruling, he suggests enquiring whether, in the light of the objectives of Regulation (EC) No 469/2009 of establishing a balanced system taking into account all the interests at stake, including those of public health, the notion of a ‘new therapeutic use’ should be assessed according to stricter criteria than those for assessing the patentability of the invention.

SANTEN asserts, conversely, that the notion of a different application within the meaning of *Neurim* should be interpreted broadly, that is to say, as including not only different therapeutic indications and diseases, but also different formulations, posologies and means of administration.

In so far as that concept of a different application cannot be interpreted with certainty, as is necessary in order to resolve the dispute, by reading the *Neurim* judgment, the Court of Appeal finds it appropriate for that purpose to refer for a preliminary ruling a question worded in accordance with the operative part of this decision.

17 Secondly, the director of the INPI is uncertain of what link there should be between the different application thus defined and the basic patent. In his decision of 19 July 2012, he found that the basic patent relied upon protects not only a new application of ciclosporin (claims 23 to 24) but also and primarily a submicron oil-in-water ophthalmic emulsion containing an active substance, including ciclosporin (claims 1 to 21 and 25 to 26). In his pleading he argues, slightly differently, that the basic patent must have the same scope as the MA relied upon and, therefore, that scope must be limited to the new medical use corresponding to the therapeutic indication in that MA.

Since it is still necessary to answer that question in order to resolve the dispute, it is still appropriate to refer for a preliminary ruling a question worded in accordance with the operative part of this decision.

The proceedings will be stayed until the Court of Justice has ruled on that question. **[Or. 10]**

ON THOSE GROUNDS

18 The Court of Appeal, ruling *inter partes*,

Refers the following questions to the Court of Justice of the European Union for a preliminary ruling:

‘1 — Must the concept of a ‘different application’ within the meaning of the judgment of 19 July 2012, *Neurim* (C-130/11, EU:C:2012:489), be interpreted strictly, that is to say:

- as limited only to the situation where an application for human use follows a veterinary application;

- or as relating to an indication within a new therapeutic scope, in the sense of a new proprietary medical product, compared with the earlier marketing authorisation, or a medicinal product in which the active ingredient acts differently from how it acts in the medicinal product to which the first marketing authorisation related;

- or more generally, in the light of the objectives of Regulation (EC) No 469/2009 of establishing a balanced system taking into account all the interests at stake, including those of public health, must the concept of a “new therapeutic use” be assessed according to stricter criteria than those for assessing the patentability of the invention;

- or must it on the other hand be interpreted broadly, that is to say, as including not only different therapeutic indications and diseases, but also different formulations, posologies and/or means of administration?

2 — Does the expression "[application] within the limits of the protection conferred by the basic patent" within the meaning of the judgment [of the Court of Justice] of 19 July 2012, *Neurim* (C-130/11, [EU:C:2012:489]), mean that the scope of the basic patent must be the same as that of the marketing authorisation relied upon and, therefore, be limited to the new medical use corresponding to the therapeutic indication of that marketing authorisation?'.

Stays the proceedings brought by SANTEN pending the ruling of the Court of Justice

[procedural references omitted]