AIPLA
American Intellectual Property Law Association

Chemical Practice Chronicles

Newsletter of the AIPLA Chemical Practice Committee

Fall 2019 Volume 7 Issue 2

In this issue:

Editors: Dolly Kao (dolly@kaoip.com)
Cristina Biggi (cristina.biggi@bugnion.eu)
R. Andrew Patty II (dpatty@mcglinchey.com)
Wan Chieh (Jenny) Lee (jlee@fkmiplaw.com)
Andrew Freistein (afreistein@wenderoth.com)

How Strict? European Court of Justice Provides Further Guidance on the Interpretation of the SPC Regulation

By Dr Beatriz San Martín, Arnold & Porter, U.K.

Introduction

Innovators in the European Union ("EU") can extend the period of exclusivity for their new medicinal products up to five years post patent expiry through the grant of a Supplementary Protection Certificate ("SPC"). Unlike US patent term extensions, an SPC does not extend the term of a patent. Instead, an SPC is a *sui generis* right, the application for which requires a patent in force and a marketing authorisation ("MA") covering the relevant product, and which only extends the period of exclusivity in relation to that product. Exactly what patents and marketing authorisations may be relied upon when applying for an SPC and what is meant by "active ingredient", "product" and "medicinal product" in the SPC Regulation[1] has vexed many and been the subject of numerous court proceedings and referrals to the Court of Justice of the European Union ("CJEU").

In this article the author provides an update on what may be understood to constitute an "active ingredient", "product" and "first authorisation" for the purposes of Article 1(b) and Article 3(d) of the SPC Regulation following the CJEU *Abraxis*[2] decision and what further questions remain unanswered in the further preliminary reference to the CJEU in the *Santen* case.

The SPC Regulation

Article 1(b) of the SPC Regulation defines "product" as the "*active ingredient or combination of active ingredients of a medicinal product*".

Article 3 of the SPC Regulation sets out the conditions that need to be satisfied in order to obtain an SPC including: (i) Article 3(b), which provides that an MA must have been granted in respect of the product; and (ii) Article 3(d), which provides that the MA referred to in Article 3(b) must be the "*first authorisation to place the product on the market as a medicinal product*".

Abraxis v Comptroller General of Patents

Abraxis markets nab-paclitaxel under the brand name Abraxane, a medicinal product indicated for the treatment of breast, pancreatic and lung cancers either on its own or in combination with other anticancer treatments under a marketing authorisation granted in 2008 (the "Abraxane MA"). Nab-paclitaxel consists of paclitaxel formulated as albumin bound nanoparticles. The addition of albumin in Abraxane has been shown to give nab-paclitaxel greater efficacy than paclitaxel and other earlier formulations already on the market under previous MAs.

In 2016, the UK Intellectual Property Office ("IPO") rejected Abraxis' SPC application for Abraxane. The hearing officer concluded on the facts that nab-paclitaxel consists of a single active ingredient (paclitaxel), together with a carrier (albumin) which enables paclitaxel to be effective in exerting its own cytotoxic effects on tumours. As a result, the Abraxane SPC application did not comply with Article 3(d) of the SPC Regulation because the Abraxane MA was not the first MA to place the

[1]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

[2]Case C-443/17 *Abraxis Bioscience LLC v Comptroller General of Patents*

product (paclitaxel) on the market. Abraxis appealed the IPO Comptroller General's decision and the appeal was heard by Mr Justice Arnold in the UK High Court.[3]

Abraxis High Court Judgment

The main thrust of Abraxis' appeal was that nab-paclitaxel is a single active ingredient rather than a combination of an active ingredient with an excipient or adjuvant – in nab-paclitaxel, paclitaxel is tightly bound to albumin and this has important therapeutic consequences. As a consequence, nab-paclitaxel is a different "product" to paclitaxel within the meaning of Article 1(b) of the SPC Regulation and therefore complies with Article 3(d).

The Comptroller General of Patents in turn argued that this was not what the hearing officer had found as a matter of fact, a conclusion which was supported by the terms of the Abraxane MA itself which referred to paclitaxel as the active component.

In his judgment, Mr Justice Arnold agreed with the hearing officer that it was clear that nab-paclitaxel is not the active ingredient of Abraxane within the meaning of Article 1(b) - paclitaxel is the active ingredient and albumin is a carrier. No further guidance from the CJEU was needed as to the interpretation of Article 1(b) since the interpretation of that provision was *acte clair*. This was because, the CJEU judgments in *MIT*[4]*, GSK*[5] and *Forsgren*[6] had made it clear that Article 1(b) should be interpreted strictly and cannot include substances that do not have a therapeutic effect on their own. Although "active ingredient" is not defined in the SPC Regulation, a strict interpretation is supported by Commission's Explanatory Memorandum proposing what became Council Regulation 1768/92/EEC (the original SPC Regulation) which states at paragraph 11 (emphasis added):

> "The proposal for a Regulation therefore concerns only new medicinal products. It does not involve granting a certificate for all medicinal products that are authorized to be placed on the market. Only one certificate may be granted for any one product, a product being understood to mean an active substance in the strict sense. Minor changes to the medicinal product such as a new dose, the use of a different salt or ester or a different pharmaceutical form will not lead to the issue of a new certificate."

Arnold J did, nonetheless, consider it appropriate to refer the following preliminary question to the CJEU on the interpretation of Article 3(d) on the issue of whether the MA for nab-paclitaxel could be considered to be the first MA under Article 3(d) of the SPC Regulation:

> "*Is Article 3(d) of the SPC Regulation to be interpreted as permitting the grant of an SPC where the MA referred to in Article 3(b) is the first authorisation within the scope of the basic patent to place the product on the market as a medicinal product and where the product is a new formulation of an old active ingredient?*"

CJEU Abraxis decision

Like Mr Justice Arnold, the CJEU considered previous case law, the Commission's Explanatory Memorandum and the rationale behind the creation of the SPC system before confirming its previous position that the definition of "active ingredient" does not extend to substances which have no therapeutic effect on their own. As such, a new formulation of an old active ingredient

---

[3]*Abraxis Bioscience LLC v The Comptroller General of Patents*, High Court of England and Wales, (Arnold J) [2017] EWHC 14 (Pat)
[4]Case C-431/04 *Massachusetts Institute of Technology* [2006] ECR I-4089
[5]Case C-210/13 *GlaxoSmithKline Biologicals SA v Comptroller-General of Patents, Designs and Trade Marks* [EU:C:2013:762], [2014] RPC 17
[6]Case C-631/13 *Forsgren v Österreichisches Patentamt* [EU:C:2015:13]

(paclitaxel) and the carrier (albumin) which has no therapeutic effect on its own is not a new product under Article 1(b) of the SPC Regulation, even if that new formulation allows the active ingredient to exercise its therapeutic effect with increased efficacy, as is the case with nab-paclitaxel.

As for the question of whether an MA for a new formulation of an old active ingredient could be regarded as being the first MA granted for that product, the CJEU firmly held that, where an MA has already been granted for an active ingredient, an MA for a new formulation of that active ingredient cannot be regarded as the first MA.

Comment

In the *Abraxis* decision, the CJEU has adopted a strict interpretation to both "active ingredient" under Article 1(b) and the condition to obtaining an SPC in Article 3(d) noting that "*the legislature intended, in establishing the SPC regime, to protect not all pharmaceutical research giving rise to the grant of a patent and the marketing of a new medicinal product, but to protect research leading to the first placing on the market of an active ingredient or a combination of active ingredients as a medicinal product*".

Interestingly, the CJEU expressly refers to the controversial *Neurim* CJEU decision in which it held that the existence of an earlier veterinary MA for the same active ingredient (melatonin branded as Regulin), did not preclude the grant of an SPC for a second therapeutic use (insomnia) of the same active ingredient (branded as Circadin) so long as that application fell within the scope of protection of the basic patent being relied upon. The *Neurim* decision was interpreted by some IP practitioners as opening the floodgates for SPCs for further therapeutic uses. However, whilst the CJEU does not criticise the *Neurim* decision, it does limit its ramifications by referring to it as an "*exception to the narrow interpretation of Article 3(d)*" which "*does not, in any event, refer to cases of new formulations of the product at issue*".

The explicit reference to the limitation of the *Neurim* decision in the *Abraxis* case may shine a light on the likely approach to be taken by the CJEU in the pending CJEU reference in the *Santen* case. Here, the CJEU has been specifically asked by the Court of Appeal of Paris to clarify whether *Neurim* should be interpreted strictly, in particular, the extent to which the concept of different MA application in *Neurim* (i) should be limited only to the situation where an application for human use follows a veterinary application; or (ii) alternatively, whether it relates more broadly to an indication with a new therapeutic use 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. In the further alternative, should *Neurim* be interpreted broadly so that it applies not only to different therapeutic indications and diseases, but also to different formulations, posologies and/or means of administration?

In *Santen,* the SPC in question relates to the active ingredient ciclosporin for use in the treatment of keratitis (an eye condition) and branded as Ikervis. The French patent office rejected the SPC application on the basis that there was an earlier MA for the same active ingredient for various therapeutic indications including indications relating to eye conditions and branded as Sandimmun. Santen argues that the earlier formulation of ciclosporin does not fall within the claims of the basic patent being relied upon and, relying on Neurim, the relevant MA should be the MA to treat keratitis.

The *Abraxis* CJEU decision already provides an answer in part to the questions raised in the *Santen* case: *Neurim* is not to be interpreted broadly and is an exception to the general proposition that Article 3(d) should be interpreted narrowly. Like *Abraxis,* the *Santen* case concerns a different formulation of the same active ingredient. However, *Santen* could be distinguished as Ikervis is used for a different indication to Sandimmun. This author anticipates that the CJEU will limit the scope of

[7]Case C-673/18 *Santen SAS v Directeur général de l'Institut national de la propriété industrielle*

the exception in *Neurim* to what is strictly necessary for the purposes of the *Santen* reference. The CJEU is likely to either restate its decision in *Abraxis* to confirm that the Ikervis MA cannot be considered as the first MA under Article 3(d) because the active ingredient is the same and preclude granting an SPC to Santen, or it will qualify its decision in *Abraxis* and allow an SPC because there is a different therapeutic use. How strict a line the CJEU will take is, however, difficult to predict.

AIPLA Chemical Practice Committee Leadership And Contact Information

Chair

Roy P. Issac, Ph.D., J.D.
Allergan PLC
roy.issac@allergan.com

Vice-Chair

R. Andrew Patty II
McGlinchey Stafford, PLLC
dpatty@mcglinchey.com

Immediate Past President

Carol Neilsen
Neilsen IP Law LLC
carol@neilsenipaw.com

Pharmaceutical Subcommittee

Kimberly Braslow
AstraZeneca
kim.braslow@astrazeneca.com

Jeremy McKown
Johnson & Johnson
jmckown@its.jnj.com

Andrina Zink
Alkermes
Andrina.zink@alkermes.com

Materials Science and Natural Resource Technologies Subcommittee

Marcus S. Simon
Dorsey & Whitney LLP
simon.marcus@dorsey.com

Law Student Subcommittee

Jill A. Hecht
University of Houston Law Center
jahecht@central.uh.edu

Jorge Zamora
University of Houston Law Center
jazamora4@central.uh.edu

Newsletter Subcommittee

Dolly Kao
Kao IP
Dolly@kaoip.com

Wan Chieh (Jenny) Lee
Fay Kaplun & Marcin, LLP
jlee@fkmiplaw.com

Cristina Biggi
Bugnion S.p.A.
cristina.biggi@bugnion.eu

Andrew Freistein
Wenderoth, Lind & Ponack, LLP
afreistein@wenderoth.com

Professional Programs Subcommittee

Thomas L. Irving
Finnegan, Henderson, Farabow, Garrett & Dunner, LLP
tom.irving@finnegan.com

Thomas J. Engellenner
Pepper Hamilton LLP
engellennert@pepperlaw.com

Beatriz San Martín
Arnold & Porter
beasanmartin@yahoo.co.uk

Microsite Subcommittee

Wan Chieh (Jenny) Lee
Fay Kaplun & Marcin, LLP
jlee@fkmiplaw.com

International Education

Matthew Barton
Forresters
mbarton@forresters.co.uk

Toby Mak, Ph.D.
Tee & Howe Intellectual Property Attorneys
toby.mak@teehowe.com