Intellectual Property Office

BL O/711/22

23 August 2022

REGULATION (EC) 469/2009 CONCERNING THE SUPPLEMENTARY PROTECTION CERTIFICATE FOR MEDICINAL PRODUCTS

APPLICANT	Roche Glycart AG
ISSUE	Whether application for supplementary protection certificate SPC/GB17/055 meets the requirements of Article 3(b) and 3(d) of the Regulation
HEARING OFFICER	Dr L Cullen

DECISION

Introduction

1 This decision relates to supplementary protection certificate (SPC) application SPC/GB17/055 ("the application") for a combination of two active ingredients, identified on the form SP1 accompanying this application as "*obinutuzumab and bendamustine, in all forms protected by the basic patent*". The application was filed in the name of Roche Glycart AG ("the applicant") on 10 October 2017[1].

2 This SPC application relies on basic patent EP(UK) 2464382 B1, entitled "*Combination therapy of an afucosylated CD20-antibody with bendamustine*". This patent discloses that the combination of bendamustine, a nitrogen mustard derivative, with an afucosylated anti-CD20 antibody, such as obinutuzumab, showed synergistic anti-proliferative effects (i.e., even more than additive) when compared to the combination of this compound with a non-afucosylated anti-CD20 antibody (e.g., rituximab). The patent was filed on 12 August 2010, with an earliest priority date of 14 August 2009, and was granted by the European Patent Office (EPO) on 3 May 2017. The expiry date of this patent is 11 August 2030.

3 The marketing authorisation (MA) provided in support of this application concerns the medicinal product "GAZYVARO"[2] and is a Type-II variation to centralised European

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[1] *This decision relates to an application for a SPC that was made in 2017. Thus, it relates to the period when the UK was part of the European Union prior to its withdrawal in 2021. As such it is necessary to apply the relevant law and case law that was in force at that time in the UK. This is set out in the decision.*

[2] *GAZYVARO is a registered trademark (RTM) in the UK.*

marketing authorisation EU/1/14/937 granted by Commission Implementing Decision C(2014)5379 of 13 June 2016. As this is an authorisation granted under the centralised procedure by the European Medicines Agency, it has to meet the requirements set down in Regulation (EC) 726/2004 for a centralised approval that will cover all EU countries[3]. This Type-II variation relates to the use of the single active ingredient identified in the medicinal product GAZYVARO, obinutuzumab, with a further active substance, bendamustine.

4 I note that this SPC application is the third application filed in the UK by the applicant in relation to this same centralised European marketing authorisation EU/1/14/937. Firstly, SPC/GB15/004 was filed on 14 January 2015 for the single active ingredient, obinutuzumab. It was subsequently withdrawn on 18 July 2017. Secondly, SPC/GB16/013 was filed on 10 March 2016 and was granted on 15 October 2020 for the single active ingredient, obinutuzumab, identified in the medicinal product GAZYVARO and based on patent EP(UK) 2380910 B1. This latter patent has not yet expired, so this granted SPC has not yet come into force in the UK. Thirdly and as noted above already, although it relates to the same MA for GAZYVARO, the present application relates to a different basic patent and is directed to a combination of active ingredients, obinutuzumab and bendamustine.

5 Throughout the examination process, the examiner has maintained that the application does not satisfy Article 3(b) of the SPC regulation[4] because the marketing authorisation provided in support of this application is not for the combination of products proposed by the applicant.

6 The examiner considers that the MA is for the single product or active substance (as defined in Article 1(b) of the SPC Regulation), obinutuzumab, and, as such, the application fails Article 3(d). The examiner found support for this view from the Commission Implementing decision authorising GAZYVARO for human use and the Summary of Product Characteristics (SmPC) annexed thereto, and from the decision of the UK Court in *Yeda UK* (see further detail below).

7 The applicant's view at its simplest is that a teleological interpretation of the SPC Regulation should allow for a so-called "*loose combination SPC*". In the applicants view, an SPC for a new loose combination of active ingredients is consistent with the purpose of the regulation because the effort, in terms of cost and time, involved in getting this combination through testing and onto market for human use is equivalent to that for a fixed combination (where the two or more components of the combination are formulated in a single delivery means and are consumed at the same time). There is further discussion below of the meaning of the terms "loose combination" and "fixed combination" in the context of the present case.

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[3] *Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency; see* CELEX number: 32004R0726; *published in Official Journal of the European Union L 136 on 30.04.2004.*

[4] *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; see CELEX Document number: 32009R0469; published in Official Journal of the European Union L 152 on 16.06.2009.*

8 Following several rounds of correspondence which failed to overcome the examiner's objection, the matter came before me, at the request of the applicant in their agent's letter of 4 January 2022, for a decision on the basis of all the papers on file. I was assisted in this task by Senior Examiner Simon Grand.

The Basic Patent - EP(UK) 2464382 B1

9 The basic patent concerns a combination therapy for the treatment of cancer, comprising an afucosylated CD20 antibody, such as obinutuzumab, with a nitrogen mustard compound, bendamustine[5]. There are two independent claims in the basic patent, claim 1 is a claim to the combination cancer treatment in the Swiss-type format and claim 6 is a claim to the combination cancer treatment in the newer post- EPC2000 format[6].

10 Claim 1 of this basic patent as granted reads:

> "*Use of an afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297, for the manufacture of a medicament for the treatment of cancer in combination with bendamustine, characterized in that said cancer is a CD20 expressing cancer and in that said antibody comprises an amino acid sequence of the variable region of the heavy chain (VH) of SEQ ID NO: 7, and an amino acid sequences of the variable region of the light chain (VL) of SEQ ID NO: 20."*

11 The applicant, in response to the official examination report date dated 13 July 2020, satisfied the examiner that obinutuzumab is an example of such an "*afucosylated anti-CD20 antibody with an amount of fucose of 60 % or less of the total amount of oligosaccharides (sugars) at Asn297"* where "*said antibody comprises an amino acid sequence of the variable region of the heavy chain (VH) of SEQ ID NO: 7 and an amino acid sequences of the variable region of the light chain (VL) of SEQ ID NO: 20"* (both of the indicated Sequence IDs are as identified in the basic patent).

12 Both the applicant and the examiner were content that the patent claims protect the combination of obinutuzumab and bendamustine.

The Issue to be Decided

13 There is a single issue to be decided in the present case.

14 Does the present SPC application meet the requirements of Article 3(b) of the SPC Regulation? In effect, is the authorisation for the medicinal product GAZYVARO which is provided in support of this application a valid authorisation to place the combination of active ingredients identified in SPC application SPC/GB17/055 onto the market in the UK?

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[5] *Bendamustine is also referred to as SDX-105. It is sold under the trade names RIBOMUSTIN or TREANDA*.

[6] *See Article 54 of European Patent Convention 2000 (EPC2000)*

15 If I find that the answer to the above question is in the negative, and that this marketing authorisation relates, not to the combination which is the subject of this SPC application, but rather to the single active ingredient obinutuzumab, it will be necessary to consider if the present SPC application meets the requirement of Article 3(d) of the SPC regulation.

The Relevant Law

The SPC Regulation[4]

16 Article 1 of the SPC Regulation defines various terms, of which Articles 1(a) and 1(b) are relevant to this decision and are reproduced below:

> *"For the purposes of this Regulation, the following definitions shall apply:*
>
> *(a)* ***'Medicinal product'*** *means any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals;*
>
> *(b)* ***'product'*** *means the active ingredient or combination of active ingredients of a medicinal product;*
>
> *(c) ….*
>
> *(d) ….*
>
> *(e) …."*

17 Article 3 of the SPC Regulation defines the conditions for obtaining a certificate (emphasis added) as follows:

> ***"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 the 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 point (b) is the first authorisation to place the product on the market as a medicinal product"***

18 Article 4 of the SPC Regulation defines the subject matter of protection provided by a certificate (emphasis added) as follows:

> ***"Within the limits of the protection conferred by the basic patent, 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 and for any use of the product as a medicinal product that has been authorized before the expiry of the certificate."***

19 Article 5 of the SPC Regulation defines the effect of the certificate and reads as follows:

> "*Subject to the provisions of Article 4, the certificate shall confer the same rights as conferred by the basic patent and shall be subject to the same limitations and the same obligations."*

Relevant Case Law

Decisions of the Court of Justice of the European Union (CJEU)

(i) Yeda CJEU

20 The decision from the Court of Justice of the European Union (CJEU) in *Yeda* (C-518/10)[7] is of particular relevance to the present case[8]. I shall refer to this case as *Yeda CJEU* to distinguish it from the Yeda decision from the UK court, which I shall refer to as *Yeda UK* (see below). *Yeda CJEU* concerned a preliminary reference from the UK courts (see *Yeda UK* below) to the CJEU which, following shortly after the judgments of this court in the *Medeva* (C-322/10)[9] and *Georgetown* (C-422/10)[10] cases, was dealt with as a reasoned order[7].

21 This referral related to Article 3(a) and how to understand "protected by the basic patent". The question referred to the Court of Justice for a preliminary ruling was:

> *"If the criteria for deciding whether a product is "protected by a basic patent in force" under Article 3(a) of … Regulation [No 469/2009] include or consist of an assessment of whether the supply of the product would infringe the basic patent, does it make any difference to the analysis if infringement is by way of indirect or*

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[7] *Yeda Research and Development Company Ltd and Aventis Holdings Inc. v Comptroller General of Patents, Designs and Trade Marks, C-518/10; For the full text of this decision see ECLI identifier* ECLI:EU:C:2011:779; CURIA - Documents (europa.eu); EUR-Lex - 62010CO0518 - EN - EUR-Lex (europa.eu);

[8] *Given the legislative framework that was in place in the UK at the time when the application for the SPC was made in 2017 (i.e., prior to exit of the UK from the European Union in 2020), the decisions of the Court of Justice of the European Union (CJEU) had a binding effect on a lower tribunal in the UK, such as the IPO, in relation to interpretation of the SPC Regulation.*

[9] *Medeva BV v Comptroller General of Patents, Designs and Trade Marks; Case C-322/10; For the full text of this CJEU decision see ECLI identifier: ECLI:EU:C:2011:773; EUR-Lex - 62010CJ0322 - EN - EUR-Lex (europa.eu); CURIA - Documents (europa.eu)*

[10] *Georgetown University and Others v Comptroller General of Patents, Designs and Trade Marks; Case C-422/10; For the full text of this CJEU decision see ECLI identifier: ECLI:EU:C:2011:776; EUR-Lex - 62010CJ0422 - EN - EUR-Lex (europa.eu); CURIA - Documents (europa.eu)*

contributory infringement based on Article 26 of the [European] Patent Convention, enacted as Section 60(2) of the [UK] Patents Act 1977 in the United Kingdom, and the corresponding provisions in the laws of other Member States of the Community?"

Having indicated that the answer to what "*protected by the patent*" means in Article 3(a) was not based on a so-called infringement test (supporting the view expressed by the Advocate-General in their opinion on this point). The CJEU in *Medeva* stated that an SPC cannot be granted for active ingredients which are not specified in the wording of the claims of the basic patent relied on in support of the SPC application. In answering the *Yeda* referral, the CJEU added a further point. i.e.

"Article 3(a) 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 precluding the competent industrial property office of a Member State from granting a supplementary protection certificate where the active ingredient specified in the application, even though identified in the wording of the claims of the basic patent as an active ingredient forming part of a combination in ***conjunction with another active ingredient, is not the subject of any claim relating to that active ingredient alone****."*

(ii) Medeva, C-322/10 and Georgetown, C-422/10

22 In relation to Article 3(b), the CJEU in both the *Medeva* and *Georgetown* cases was asked to consider the following question (see Question 6 from *Medeva* and Question 1 from *Georgetown,* as referred):

"Does … Regulation [No 469/2009] and, in particular, Article 3(b), permit the grant of a [SPC] for a single active ingredient or combination of active ingredients where:

(a) a basic patent in force protects the single active ingredient or combination of active ingredients within the meaning of Article 3(a) of the SPC Regulation; and

(b) a medicinal product containing the single active ingredient or combination of active ingredients together with one or more other active ingredients is the subject of a valid authorisation granted in accordance with Directive 2001/83/EC or Directive 2001/82/EC which is the first [MA] that places the single active ingredient or combination of active ingredients on the market?"

The CJEU summarised this question, referred from the UK courts, as follows:

"By its question, the Court of Appeal asks, in essence, whether Article 3(b) of Regulation No 469/2009 may be interpreted as not precluding the competent industrial property office of a Member State from granting a SPC for a combination of two active ingredients, corresponding to that specified in the wording of the claims of the basic patent relied on, where the medicinal product for which the MA is submitted in support of the SPC application contains not only that combination of the two active ingredients but also other active ingredients."

In *Medeva,* this court then went on to provide the answer to this question as follows (my emphasis added in bold):

> *"Article 3(b) of Regulation No 469/2009 must be interpreted as meaning that, provided the other requirements laid down in Article 3 are also met, that provision does not preclude the competent industrial property office of a Member State from granting a SPC for a combination of two active ingredients, corresponding to that specified in the wording of the claims of the basic patent relied on,* ***where the medicinal product for which the MA is submitted in support of the SPC application contains not only that combination of the two active ingredients but also other active ingredients****."*

In the related *Georgetown* judgement, the court answered this question as follows (my emphasis added in bold)::

> *"Article 3(b) 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, provided the other requirements laid down in Article 3 are also met,* ***that provision does not preclude the competent industrial property office of a Member State from granting a supplementary protection certificate for an active ingredient specified in the wording of the claims of the basic patent relied on, where the medicinal product for which the marketing authorisation is submitted in support of the supplementary protection certificate application contains not only that active ingredient but also other active ingredients.****"*

23 The CJEU set out its reasons for coming to this view in paras 29-42 of its judgment in *Medeva* and in paras 24-35 of its judgment in *Georgetown* – and, although each of these judgments were issued separately, the same points were made in both regarding the answer to this question. The following points made by the CJEU are relevant in the present case:

- medicinal products for complex diseases, often consist of combinations of active ingredients for multiple therapeutic uses which can be administered to patients in a single preparation. This helps with patient compliance and reduces frequency of administration, e.g., by injection, to a minimum;

- In the specific case of vaccines, these are often developed, in particular having regard to the recommendation of the health authorities of the Member States, in the form of multivalent vaccines (which treat more than one therapeutic condition);

- If the holder of the basic patent relating to an innovative active ingredient or an innovative combination of active ingredients were to be refused a SPC on the basis that, in the commercial version of the medicinal product which places either of these on the market for the first time, the active ingredient or the combination coexists in the medicinal product alongside other active ingredients or combinations of active ingredients which have other therapeutic purposes and may or may not be protected by another basic patent in force, the fundamental objective of the SPC Regulation (which is to ensure sufficient protection to encourage pharmaceutical research and play a decisive role in the continuing improvement in public health) could be undermined;

- The consequences of this situation would be that:

(a) the holder of such a patent would enjoy only the period of effective protection conferred by the patent and this is insufficient to cover the investment put into pharmaceutical research; this is why the regulation to provide a SPC for medicinal products was created in the first place;

(b) such an approach would tend to favour the development of monovalent medicinal products, in particular vaccines, which may not be in the interests of patients or national public health authorities;

The consequence of (a) and (b) is that the holders of such patents would be forced to develop commercially, and maintain on the market, medicinal products containing only the active ingredients specified in the basic patent in order to obtain a MA for a medicinal product precisely covering those active ingredients which, as such, the holder could be certain would confer entitlement to a SPC. The CJEU concluded that such an outcome "*cannot be compatible with the fundamental objectives pursued by the SPC Regulation*.";

- Thus, the CJEU considered that, as the regulation requires that it is the '*product'* that must be covered, and not the medicinal product, by a MA then this does not in itself rule out the possibility that the MA may cover other products in such a medicinal product. As Article 4 of the regulation makes clear, the SPC is intended to protect the 'product' covered by the MA, not the medicinal product as such;

- This was supported by the explanatory memorandum to the SPC regulation, at paragraphs 34 and 39, which states that the requirement that the product must have obtained a valid MA is met, firstly, '*if the proprietary medicinal product containing it has been granted the [MA] concerned*' and, second, that in such a situation, '*where the product authorised consists of a combination of compound X and another active ingredient, only compound X will be protected by the certificate'*;

- An SPC thus granted in connection with such a product confers, in accordance with Article 5 of the regulation, upon expiry of the patent, the same rights as were conferred by the basic 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 regulation. Thus, if, during the period in which the patent was valid, the patent holder could oppose, on the basis of this patent, all use or certain uses of this 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 the certificate.

UK Court decision

Yeda UK

24 The most relevant UK authority is the decision which resulted in the above-mentioned referral to the CJEU. This case, which I shall refer to as *Yeda UK*[11], was a decision from the UK Patents High Court on appeal from a decision of the Intellectual Property Office (IPO)[12].

25 The applicant had filed two SPC applications, the first for cetuximab and the second for cetuximab and irinotecan in combination. The same marketing authorisation (MA) was cited in support of both applications and this MA related to '*Erbitux-cetuximab'*. However, in the MA there was discussion of how Erbitux-cetuximab could be used in conjunction with another therapeutically active compound, irinotecan, to treat certain types of cancer. The applicant argued that this was sufficient basis to provide support for a SPC for the combination of cetuximab with irinotecan. The court confirmed the view of the hearing officer at the IPO that the medicinal product Erbitux and its single active ingredient cetuximab was clearly defined as the subject matter of the authorisation. Although there were brief references to the use of another therapeutically active compound irinotecan with cetuximab in the MA, the Court found that these references were wholly insufficient to amount to a marketing authorisation for a product consisting of both cetuximab and irinotecan. In this example, the cetuximab and irinotecan were administered separately.

26 I shall refer to the issues discussed in this judgment that are relevant to the present case as they arise below.

Argument and Analysis

27 Before turning to consider the arguments from the applicant in this case, I think it is helpful to consider the terms being used to refer to different types of combinations in the present case to ensure there is a consistent understanding:

Types of Combinations

28 In the correspondence in this case and at the oral hearing, reference has been made to 'loose combinations of active ingredients' and to 'fixed combinations of active ingredients' and it is relevant to consider the meaning of these terms.

29 The term 'loose combination' was firstly referred to by the applicant in their letter dated 12 October 2017 filed in conjunction with form SP1 when making this SPC application.

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[11] Yeda Research and Development Co Ltd v Comptroller General of Patents [2010] (EWHC) 1733 (Pat); For full text of the this decision from UK Patents Court see Yeda Research and Development Company Ltd v Comptroller General of Patents [2010] EWHC 1733 (Pat) (12 July 2010) (bailii.org) (http://www.bailii.org/ew/cases/EWHC/Patents/2010/1733.html).

[12] For text of the IPO decision, see Imclone Systems Inc. and Aventis Holdings Inc.'s application (BL O/066/10) of 23.02.2010 here (on IPO patents decision database).

The applicant has also used the terms 'non-fixed dose combination products' and 'loose drug combination'. I consider that all of these terms refer to the same thing. I will use the term 'loose combination' to identify the situation where what is being referred to is a combination made up of two or more components, each of which is administered separately and does not form part of single delivery means, such as a tablet or solution to drink or one to be injected. Thus, in a loose combination of two components, A and B, each can be administered either at the same time or with some delay between them. They can be administered in different forms, e.g. A could be as a tablet and B could be as a solution. The amount of A and B administered relative to each other can be varied or changed depending on the patient and the condition being treated.

30 The above is in contrast to, what I shall refer to as, a 'fixed combination' which is where the components of the combination are administered at the same time and in the same form, e.g., components A and B are formulated into a single tablet and are both taken at the same time. The HPV vaccine, Gardasil[13], or HIV drug treatment, Atripla[14], are examples of fixed combination products.

31 The combination of obinutuzumab and bendamustine proposed by the applicant in the present application is an example of a loose combination. There is no overlap between the components of this combination, the bendamustine is kept separate and administered separately from the obinutuzumab. Also, it appears that the amount of each component varies from patient to patient and over time for each individual patient. Thus, it is important to note that a loose combination of the type referred to by the applicant is not a combination in the physical sense.

Argument

32 I will first summarise the main points made in the argument presented by the applicant and that presented by the examiner, before going on to provide my analysis and conclusions regarding the issue to be decided.

The Applicant's View

33 The applicant's view, at its simplest, is that a teleological interpretation of the SPC Regulation should allow an SPC to be granted for a loose combination that represents a new combination of active ingredients, because the effort involved in getting such a loose combination through testing and on to the market is equivalent to that for a fixed combination.

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[13] For further details see marketing authorisation for Gardasil at Gardasil | European Medicines Agency (europa.eu). Gardisil provides 4 active ingredients in a suspension which are administered together in a single injectable suspension to vaccinate against 4 strains of human papillomavirus

[14] For further details see marketing authorisation for Atripla at Atripla | European Medicines Agency (europa.eu). Atripla provided 3 active ingredients in a single film coated tablet which was taken orally to treat human immunodeficiency.

34 In their letter of 12 October 2017, the applicant introduced the situation regarding loose combinations as follows:

> *"generally speaking, fixed dose combination products are issued a separate marketing authorisation to a single marketing authorisation. However,* ***non-fixed dose combination products are usually issued a marketing authorisation by way of a Type II variation of a single product authorisation where there has previously been a single product authorisation, which is the case here****."*

35 The applicant, referring to the chapter concerning SPCs in the IPO Manual of Patent Practice[15], argues that a new SPC may only be granted for a combination of (a) an active ingredient for which a certificate has already been granted with (b) one or more other active ingredients, if the combinations are themselves the subjects of separate patents and combinations are specifically identifiable from the respective patent as viewed by the person skilled in the art at the priority or filing date. This is the test set out in *Teva* (C-121/17)[16]. The applicant suggests that this is clearly the case here. They assert that while the medicinal product 'GAZYVARO' only physically contains the antibody obinutuzumab, the requirements of Article 3(b) of the SPC Regulation have clearly been met, as evidenced by the fact that the SmPC for GAZYVARO explicitly states that it is mandatory that the antibody obinutuzumab is used in combination with the anti-neoplastic agent bendamustine for the treatment of non-Hodgkin lymphoma (see Type-II-variation to marketing authorisation; see section 4.1 of SmPC, which deals with therapeutic use). Thus, the applicant suggests in this context, it is immaterial that the two active ingredients are not physically formulated as a single fixed dosage form.

36 The applicant continues, in their agent's letter of 16 June 2021:

> *"In summary, therefore, the combination of active ingredients which is subject matter of the present SPC application are distinct physical entities. This has been necessitated by the required i.v. infusion regimen, which precludes the approval of a fixed dose combination or a single combination package. Nevertheless, although the two active ingredients physically only contain a single active ingredient, they have been approved to be used in conjunction. As such, here the 'product' within the meaning of the SPC Regulation is the specific mandatory combination as set out in Section 4.1 of the mentioned SmPCs, respectively".*

37 Thus, it is argued:

> *"There is no logical justification why significant clinical research resulting in a fixed combination of active ingredients should be awarded extended SPC protection, whereas loose drug combinations, which by virtue of kinetic, toxicological or other therapeutic/pharmaceutical considerations must be administered separately or sequentially, should not be entitled to an SPC. Indeed, such an arbitrary distinction is clearly contrary to the concept and principles of the SPC Regulation, which is to foster clinical research and to reward the*

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[15] *See chapter entitled "Supplementary Protection Certificates for Medicinal and Plant Protection Products" in the IPO Manual of Patent Practice (MoPP) at* ***Manual of Patent Practice - Supplementary Protection Certificates for Medicinal and Plant Protection Products - Guidance - GOV.UK (www.gov.uk).*** *The MoPP explains the IPO's practice in relation to SPCs under the Patents Act 1977.*

[16] See *Teva UK Ltd. and others (trading as 'Mylan') v Gilead Sciences Inc., C-121/17; For full text of this decision see ECLI identifier: ECLI:EU:C:2018:585; EUR-Lex - 62017CJ0121 - EN - EUR-Lex (europa.eu); CURIA - Documents (europa.eu)*

applicant with an SPC where a marketing authorisation is obtained for a new product."

38 The applicant notes that the *Yeda UK* decision predates the CJEU decisions in *Medeva* and *Georgetown*. The applicant discussed how, prior to *Medeva,* the competent bodies responsible for granting SPCs took the standpoint that the basic patent should be commensurate with the active ingredients contained in the approved medicinal product (i.e., the 'product' in accordance with Article 3(a) should be commensurate with the product of Article 3(b)). Such a literal interpretation of Articles 1 to 3 of the SPC Regulation resulted in member states rejecting an SPC request if the approved medicinal product contained more active ingredients than those claimed in the basic patent. The restrictive interpretation of the term 'product' within the meaning of Articles 3(a) and (b) of the SPC Regulation however had the consequence of effectively precluding the issue of an SPC for products which, due to commercial or therapeutic considerations, must be approved in a combination with other active ingredients. The applicant considers that this was resolved by the CJEU taking a teleological approach in its *Medeva* and *Georgetown* decisions, where the CJEU ruled that an SPC can be granted for an active ingredient or a combination of active ingredients, even if the medicinal product of the marketing authorisation relied upon also contains further additional active ingredients. As set out in paragraphs 34 to 36 of *Medeva*, such an approach is compatible with the fundamental objectives of the SPC Regulation.

39 The approach outlined in *Medeva* provides SPC protection for manufacturers of medicinal products who are obliged, for legal or practical reasons, to market an active ingredient as a fixed combination with other active ingredients. The applicant notes that many therapeutic regimens for the treatment of a disease require the use of a combination of active ingredients. They argue that the CJEU in *Medeva* and *Georgetown* has recognised that, at least in the case of fixed combinations, it is not detrimental that the medicinal product approved contains more active ingredients than those defined in the SPC request or claimed in the basic patent. I consider that this is a relevant point to note and I will return to it again below.

40 They further note that, just as it is necessary in some therapeutic fields, such as in the field of vaccines as considered by *Medeva*, for practical reasons to seek approval of multiple active ingredients in a medicinal product as a fixed dosage form, so in other therapeutic areas, combinations by way of a fixed dosage form of active ingredients may not be feasible or practical. This is the case particularly if, as in the present application, continuous dose modifications of the active ingredients are necessary in order to optimise therapy and to minimise adverse reactions in the individuals being treated. Such active ingredients, although destined to be used in conjunction with each other, the applicant points out must therefore be formulated as a separate, 'loose' combination dosage form. The applicant argues that, in such a situation, the mandatory combined use of the active ingredients may nevertheless be clear from the SmPC for the medicinal product, which is a central part of the marketing authorisation. The applicant further notes that it is very well established that what they refer to 'as such a personalised medicine approach' has potentially immense therapeutic advantages, as it allows tailoring therapy with the best response and highest safety margin to ensure better patient care.

41 They go on to assert that the development of such 'loose' combination therapies are just as cost intensive and time consuming as the development of other innovative medicinal products, and assert that on a balance of interests, it is self-evident that there is no logical justification in denying such products additional supplemental protection. I note that these points were asserted by the applicant rather than supported by any written materials or submissions.

42 Thus, the applicant concludes that the principles of *Medeva* which provides for SPCs for fixed combinations, as a corollary should be equally applicable to what they consider is the reverse case, namely where an SPC is sought for a combination of active ingredients as identified in the claims of the basic patent and where the approved medicinal product, while only physically containing one of the claimed active ingredients, is in accordance with the SmPC to be used in conjunction with a further specific active ingredient, that is identified in the patent.

43 As with vaccine products, the applicant considers that there are sound reasons why the refusal to grant a SPC in the present case would undermine the objective of the SPC Regulation and discriminate against research where combination products can only be formulated as a loose combination. Again, this was asserted in my view but was not supported by any written materials or submissions

44 They argue that the present case reflects a situation akin to that which arose in *Medeva* and *Georgetown*, i.e., "*this is a situation where the patentee falls between two stools and is not entitled to an SPC*". In *Medeva* and *Georgetown*, this was remedied by the CJEU adopting a teleological interpretation, and the same should be done here. This may be achieved, they assert, by treating the marketing authorisation not literally as the approval for a medicinal product including obinutuzumab as active ingredient; but instead regarding it teleologically as being, in effect, three marketing authorisations which all share one active ingredient in common – the three authorisations would thus be for (i) obinutuzumab; (ii) obinutuzumab and chlorambucil, and (iii) obinutuzumab and bendamustine.

45 Furthermore, in view of the update to the MA by the Type-II variation to include the obinutuzumab and bendamustine combination, which required, in the view of the applicant, much safety and efficacy testing to achieve, they believe that the variation granted on 13 June 2016 "*should essentially be seen as giving eligibility as the first marketing authorisation for the product obinutuzumab and bendamustine*". In effect they consider that the date of the variation and not the date of the original marketing authorisation for obinutuzumab should be the date used for determining when the MA took effect and the duration of any SPC based on it (under Article 13 of the SPC regulation)[4]. They further assert that the fact that a separate patent was granted for this combination is a further indication that this is a separate innovative product, warranting its own SPC protection.

The Examiner's View

46 The examiner maintained the same objection throughout, namely that the application does not comply with Article 3(b) of the SPC regulation because the marketing authorisation provided in support of the application is not a valid UK authorisation to place the product on the market. The examiner argues that this marketing authorisation only allows the single active ingredient obinutuzumab to be placed on

the market. They found support for this view in the fact that the Implementing Decision issued by the European Commission granting the MA refers only to obinutuzumab and that obinutuzumab alone is indicated as the active ingredient in section 2 of the SmPC annexed to this implementing decision. The use of obinutuzumab with bendamustine is only proposed as a therapeutic indication in section 4 of the SmPC dated 13 June 2016.

47 The Commission Implementing Decision for GAZYVARO is entitled as follows:

> *"COMMISSION IMPLEMENTING DECISION of 13.6.2016 amending the marketing authorisation granted by Decision C(2014)5379(final) for 'GAZYVARO – obinutuzumab', an orphan medicinal product for human use".*

Thus, it identifies both the medicinal product and the product that the implementing decision relates to. Section 2 of the SmPC entitled "2. QUALITATIVE AND QUANTITATIVE COMPOSITION" states clearly (my emphasis added below in bold):

> *"One vial of 40 mL concentrate contains 1,000 mg* ***obinutuzumab,*** *corresponding to a concentration before dilution of 25 mg/mL.* ***Obinutuzumab is a Type II humanised anti-CD20 monoclonal antibody of the IgG1 subclass derived by humanisation of the parental B-Ly1 mouse antibody and produced in the Chinese Hamster Ovary cell line by recombinant DNA technology****. …"*

Section 4 of the SmPC entitled "4. CLINICAL PARTICULARS" contains a number of sections, i.e.:

- section 4.1 which deals with therapeutic use;
- section 4.2 which deals with posology and methods of administration;
- section 4.3 which deals with contra-indications; and
- section 4.4 which deals with special warnings & precautions for use.

of which, section 4.1 which is entitled "**Therapeutic indications**", reads as follows:

> *"…Gazyvaro in combination with bendamustine followed by Gazyvaro maintenance is indicated for the treatment of patients with follicular lymphoma (FL) who did not respond or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen."*

48 The examiner also noted that, although the applicant had clearly conducted safety and efficacy studies for what they identify as the loose combination product (see page 4 of the attorney's letter dated 10 October 2017), the marketing authorisation does not facilitate the holder to place such a combination on the market for human use. The MA does not provide the same amount of information on the bendamustine active ingredient as it does on the obinutuzumab active ingredient.

49 The basis of the examiner's view is the decision of UK court in *Yeda UK* and the reasoning in the decision of the CJEU in *Yeda CJEU.* In *Yeda UK* at paragraph 26, discussing the decision granting the MA for 'Erbitux-cetuximab', the court stated:

> *"So far as the first point is concerned, article 1 of the decision plainly identifies the medicinal product, "Erbitux – cetuximab" as the subject-matter of the authorisation. No other medicinal product is identified. The direction to enter that product in the Community Register of Medicinal Products is to the same effect.*

Article 3 specifies the form of the labelling and package leaflet. The outer packaging makes no mention of irinotecan at all. The package leaflet contains two brief mentions of irinotecan in explaining how cetuximab is used. The summary of the product characteristics likewise contains brief mentions of irinotecan in explaining how cetuximab is used. But as the case law shows, how a medicinal product is used does not form part of the identification of the product itself. In my judgment the brief references to irinotecan in explaining how cetuximab is used are wholly insufficient to amount to a marketing authorisation of a product consisting of both cetuximab and irinotecan. In short, I agree with the Hearing Officer for the reasons that he gave."

The examiner considers that the same situation arises in relation to the MA for 'Gazyvaro- obinutuzumab'.

50 In making this argument, the examiner considered that there was implicit support for their position from the *Yeda CJEU* decision. They argued that the CJEU approved the position put forward by the UK national court in *Yeda UK*. They noted that in *Yeda CJEU* the court did not rule on Article 3(b) because that had already been determined in light of the judgements in *Medeva* and *Georgetown*. The court provided an additional clarification in relation to Article 3(a). The examiner considered that this points to the fact that the CJEU approved the approach from the UK court and considered there was no reason to propose that the approach to Article 3(b) should be any different to that already mentioned & discussed in *Medeva* and *Georgetown*. This, the examiner considers, provides tacit support for their argument that *Yeda UK,* by virtue of *Yeda CJEU* confirming Medeva & Georgetown, is relevant to determining whether (or not) the present application meets the requirements of Article 3(b).

Analysis

51 The key to this decision is whether the marketing authorisation provided in support of this application is a marketing authorisation for two active ingredients, obinutuzumab and bendamustine, or a marketing authorisation to one active ingredient alone, obinutuzumab.

52 As set down in the Withdrawal Agreement from the EU and as explained recently in office decision *Janssen Biotech Inc's Application* (BL O/242/22)[17], the IPO as a tribunal is bound by all of the decisions of the CJEU concerning SPCs delivered prior to the end of the Withdrawal Period. As a result, I am bound by the decisions made in the *Medeva*, *Georgetown* and *Yeda CJEU* cases mentioned already as well as that made in *Santen C-673/18* (see below)[18]. As stated in *Medeva*, see para 30-32, the fundamental objective of the SPC Regulation is to ensure sufficient protection to

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[17] *See IPO decision BL/O242/22, Janssen Biotech Inc's application, concerning SPC application SPC/GB17/023 see especially paras 46-53 (Patent decision O/242/22 (ipo.gov.uk).*

[18] *Santen SAS v Directeur Général de l'Institut National de la Propriété Industrielle (INPI); Case C-673/18. For the full text of this CJEU decision see ECLI identifier: ECLI:EU:C:2020:531; EUR-Lex - 62018CJ0673 - EN - EUR-Lex (europa.eu), CURIA - List of results (europa.eu)*

encourage pharmaceutical research and play a decisive role in the continuing improvement in public health and to address the fact that the period of effective protection under the patent is insufficient to recoup the investment put into pharmaceutical research; thus the protection conferred by a SPC is largely intended to cover the cost of research leading to the discovery of new 'products'. For the purpose of SPCs we are concerned with the products or the active ingredients.

53 As the decision in *Medeva* made clear and, as I have summarised above, the fact the SPC relates to the product(s) and not the medicinal product was influential in the CJEU concluding that the SPC could be granted for an active ingredient or combination of active ingredients which "*coexists in the medicinal product alongside other active ingredients or combinations which have other therapeutic purposes and may or may not be protected by another basic patent in force".* Unlike the situation in *Medeva*, *Georgetown* and *Yeda UK*, there is no Article 3(a) question at issue in the present case. It is accepted that the combination of active ingredients for which the SPC is being sought is specified in the wording of the claims of the relevant basic patent. Thus, whilst I fully accept that the SPC Regulation should be approached in a teleological fashion rather than a purely literal one, it is also true that when considering the purpose and objectives of the relevant EU legislation, one cannot ignore the wording of the articles in question. In order to satisfy Article 3(b), the authorisation provided in support of the SPC applied for in the present case must allow one to place the product, in this case the combination of obinutuzumab and bendamustine, on the market as a medicinal product.

54 In *Medeva* and *Georgetown,* the authorised medicinal product in both cases included the combination of active ingredients in question as part of the list of ingredients in the medicinal product. This is not the case in the present case, the medicinal product only contains obinutuzumab.

55 I consider that the examiner has correctly identified that the marketing authorisation does not describe the combination of obinutuzumab and bendamustine. While I accept that, as the applicant has pointed out, there is an explanation of how obinutuzumab can be used with other therapeutically active compounds and treatments, this is only in one part of the MA and only in relation to the discussion on clinical use. The applicant appears to disregard the fact that the MA is more than just the section describing clinical use (often titled 'clinical particulars'), albeit that this is an important one. For example, the SmPC also provides information on the composition and formulation of the medicinal product; the pharmacological properties of the active ingredient; what additional ingredients make up the medicinal product and what their purpose is; and what are the outcomes from all the testing that was carried out on obinutuzumab. There is not the same level of information provided about the other components in either of the combinations involving other active ingredients referred to by the applicant; and which are discussed in the clinical section of the SmPC – i.e., that with bendamustine or that with chlorambucil. It would appear to be necessary to go to some other source, e.g., a different marketing authorisation document, to find the same level of information about bendamustine or chlorambucil, that the present MA provides in relation to obinutuzumab.

56 Further, I draw support for this view from the fact that the clinical particulars section also includes details on the use of obinutuzumab (as the medicinal product GAZYVARO) in combination treatment involving chemotherapy (it does not provide

further details of the chemotherapy regime that would be necessary) and also it indicates that, after the initial combination of obinutuzumab and chemotherapy, there would be subsequent use of GAZYVARO on its own as maintenance therapy. Taken together with, and being bound by, the earlier decision from the UK court in *Yeda UK*, I am not persuaded by the applicant's arguments on how to consider the MA in present case teleologically as approving 3 products rather than just 1 product.

Relevance of CJEU decisions in Medeva and Georgetown

57 Allowing an SPC to be granted for a combination of active ingredients covered by a basic patent which forms part, but not all, of the medicinal product that is the subject of a marketing authorisation seems to me to be quite different to allowing an SPC to be granted for a combination of active ingredients covered by a basic patent but where not all of these active ingredients are the subject of the marketing authorisation. I do not consider that this is merely the corollary of the situation in *Medeva* and *Georgetown* as described by the applicant, I consider that it is a fundamentally different approach. It would require me to look at the marketing authorisation provided in support of this SPC application in a very different way. I do not believe that I am free to view marketing authorisation EU/1/14/937 as the applicant proposes, i.e., as a document that authorises a series of products with effect from different dates, i.e., a single product and a number of combination products which appear to have one common active ingredient which were authorised by variation of the original authorisation. I consider that it is more logical to view the MA as the document that authorises a medical product comprising a single active ingredient obinutuzumab, which provides the details of what obinutuzumab is and what effect it has clinically and how it is used to achieve a therapeutic effect. I consider that this is a single authorisation for obinutuzumab that discusses different ways in which obinutuzumab can be used in therapy. I do not consider that it is a multiple authorisation for (i) obinutuzumab on its own; (ii) a combination of obinutuzumab with bendamustine and (iii) a combination of obinutuzumab with chlorambucil. Article 1 and Article 3(b) indicate that the authorisation approves the placing of a medicinal product comprising the active ingredients (or combination of active ingredients) on the market. In this case, one of the components of the combination for which the SPC is being sought is not part of the medicinal product covered by the marketing authorisation. Thus, I do not think that the term 'loose combination' used by the applicant is helpful here. I think that the clinical particulars of the SmPC associated with the MA indicate how a medicinal product comprising obinutuzumab as a single active ingredient can be used with other active ingredients or other forms of therapy. However, this does not mean, in my view, that it also provides all the information necessary to place a combination product including obinutuzumab onto the market as a medicinal product. I do not believe that I can ignore the fact that there needs to be relationship to the medicinal product. It is the active ingredient in this medicinal product that has been approved, not an active ingredient that is the medicinal product and, potentially any other active ingredient that is not in this medicinal product!

58 If I take the approach suggested by the applicant the logical conclusion is that a marketing authorisation may give rise to any number of combinations all of which would appear to take affect from different dates as they would each most likely be the subject of a Type-II variation. Furthermore, the fact that this section of the SmPC does not just refer to the use of obinutuzumab with other active components (bendamustine,

chlorambucil), but it also includes the details of obinutuzumab in use in combination with other forms of therapy such as chemotherapy as noted above, points to the interpretation that this section describes how obinutuzumab is used in a variety of different therapeutic actions and not a number of different combinations of obinutuzumab with other active ingredients, each of which can be placed on the market as a medicinal product based on this MA.

59 While I note that the applicant questions its relevance in the present case given that *Yeda UK* was decided before the CJEU decisions in *Medeva* and *Georgetown*, as I have explained above, the CJEU did actually consider the referral from the UK court in its *Yeda CJEU* decision which took account of the *Medeva* and *Georgetown* judgments when deciding to issue its decision as a reasoned order. Indeed, paras 30-32 of *Yeda CJEU* discuss the relevance of *Medeva* to dealing with the issues in this case.

60 The applicant, in the agent's letter of 16 June 2021, makes a number of points concerning how they regard the judge in the *Yeda UK* decision as having erred. However, I consider that these points do not provide me with any basis on which I can find that the conclusions and implications of the *Yeda UK* and *Yeda CJEU* decisions can be ignored or distinguished from the present case. In acting in my role as hearing officer at the IPO, which is a lower tribunal to the Patents Court, I cannot disregard case law from the higher tribunals by which I am bound.

Need for Loose Combinations

61 The applicant argues that if as in the present situation, practical considerations mean that combinations by way of a fixed dosage form of active ingredients may not be feasible, they should not be prevented from obtaining an SPC for a loose combination which overcomes the practical considerations working against a fixed dose solution. The applicant further argues that it is very well established that the use of 'loose combinations' provides a personalised medicine approach that has potentially immense therapeutic advantages, as it allows tailoring therapy with the best response and highest safety margin to ensure better patient care. The applicant also asserts in my view that the development of such 'loose' combination therapies are just as cost intensive and time consuming as the development of other innovative medicinal products, and it is self-evident that there is no logical justification in denying such products additional supplemental protection.

62 However, I do not consider that these points are persuasive. In my view they are asserted. The applicant did not provide any documents or material to support these points in the present case.

63 The analogy that the applicant draws from the *Medeva* and *Georgetown* decisions which relates to medicinal products comprising subset combinations of active ingredients that had a number of therapeutic impacts and an SPC can be obtained for each subset is not persuasive in my view. The present situation is not one where there are a number of active ingredients in the authorised medicinal product which provide treatment for a number of therapeutic conditions and the SPC being sought relates to a subset of those active ingredients that are dedicated to one specific therapeutic use (of this multivalent product, for example, a vaccine such as was discussed in *Medeva* – see para 39 above). In the present situation, we have only one active ingredient

(obinutuzumab) identified in the medicinal product (Gazyvaro) with one therapeutic activity (leukaemia). The other active component identified is not part of the medicinal product (i.e., chlorambucil or bendamustine). I find that I am in agreement with the view expressed by the examiner, there is still only one active ingredient (obinutuzumab) in the medicinal product GAZYVARO.

64 I accept that all active ingredients that will be used to exert a therapeutic effect on humans need to be tested and if they are being used in combination with other active ingredients these need to be tested alone and in combination as well. The results of such tests will have to be provided to the authorities responsible for authorising the product in order to determine if they provide an appropriate risk-to-benefit profile. However, I do not consider that the present marketing authorisation provides all the data for the combination of obinutuzumab and bendamustine, it appears to me that there is a lot of information about the bendamustine that is not provided in the present application which is provided for the obinutuzumab. Accordingly, I do not place the same significance as the applicant does on the fact that the present SmPC shows, what the applicant states is, the "*mandatory combined use of the active ingredients*". In my view the marketing authorisation tells you what other active ingredients you can effectively use with obinutuzumab (in the form of GAZYVARO) but does not provide an authorisation to do so.

Relevance of CJEU decisions in Neurim & Santen and case-law from the Austrian Court

65 I note that the applicant initially relied upon a decision from the Austrian Court (decision 34 R 104/15 of the Higher Regional Court of Vienna) that drew on the CJEU decision in *Neurim (C-130/11)* to support their suggested teleological interpretation*,* but they subsequently stepped away from this argument. In their correspondence, dated 16 June 2021, the applicant stated that:

> "*For these reasons [those in relation to* Medeva *etc discussed above],* Santen *and* Neurim *are not applicable to the present facts and situation, and in the light of the established case law in* Medeva/Georgetown*, we should be entitled to an SPC."*

They further stated that:

> "*Whilst we appreciate that the Austrian court had relied on* Neurim*, we still believe that the facts of our case are different due to the fact that the product is a new combination product, albeit a loose one, not a new indication of an existing product."*

I take this to mean that the applicant believes that the Austrian court made the correct decision, but that they no longer consider that the reasoning of this court in doing so is relevant to the present application. As a result, I will not consider the Austrian Court decision further for the purposes of the present decision.

66 However, I do think it is useful to take account of the *Santen* judgment and note the following points regarding the CJEU's position in this judgment. The examiner noted that, following the decision in *Santen*[17], it was no longer tenable to rely on the notion of a first relevant marketing authorisation, as previously identified in the *Neurim* decision from the CJEU, as the therapeutic indication was no longer a consideration

in identifying the first relevant patent. The operative part of the *Santen* judgment states (my emphasis added in bold):

> "*Article 3(d) 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* ***a marketing authorisation cannot be considered to be the first marketing authorisation, for the purpose of that provision, where it covers a new therapeutic application of an active ingredient, or of a combination of active ingredients, and that active ingredient or combination has already been the subject of a marketing authorisation for a different therapeutic application****."*

67 Therefore, I do not need to come to a conclusion on whether the Type-II variation to the MA for obinutuzumab, indicating that obinutuzumab can be used effectively with bendamustine, amounts to a new therapeutic application or the first relevant marketing authorisation as this concept cannot now provide a route to an allowable SPC. Instead, the applicant now states that they regard the use of bendamustine with obinutuzumab as a new combination.

68 The *Santen* judgment[17], drawing on the earlier CJEU decision in *Abraxis* C-443-17[19], also states that Article 1(b) of the SPC regulation is to be interpreted strictly. Paragraph 51 of the *Santen* judgment states:

> *"In addition, in the light of the strict definition of the term 'product' within the meaning of Article 1(b) of Regulation No 469/2009, as is apparent from paragraphs 40 to 45 above, the analysis of the wording of Article 3(d) of that regulation presupposes that* ***the first MA for the product as a medicinal product for the purpose of that provision means the first MA for a medicinal product incorporating the active ingredient or the combination of active ingredients at issue*** *(see, to that effect, judgment of 21 March 2019, Abraxis Bioscience, C-443/17, EU:C:2019:238, paragraph 34),* ***irrespective of the therapeutic application of that active ingredient, or of that combination of active ingredients, in respect of which that MA was obtained.****"*

69 This is relevant because the applicant is asking me to disregard the UK court decision in *Yeda UK* as out of step with subsequent CJEU decisions. In this context the wording of paragraph 19 in *Yeda UK* is instructive. Here the judge stated (my emphasis):

> *"****To my mind it is clear from recital (10) and from the case law that what constitutes a 'product' is to be strictly construed****: Generics (UK) Ltd v Daiichi Pharmaceutical Co Ltd [2009] EWCA Civ 646, [2009] R.P.C. 23, CA.* ***In deciding what is a "product" one must focus****, as the hearing officer put it****, 'on what the product is, rather than what it does'****. As the ECJ said in Case C-202/05 Yissum Research and Development Co v Comptroller-General (§ 18):* ***'It follows that the concept of 'product' cannot include the therapeutic use of an active ingredient protected by a basic patent'****."*

70 Whilst not dealing with the issue of whether a teleological approach to the SPC Regulation should allow loose combinations, this statement from the UK court is very

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[19] *Abraxis Bioscience LLC v Comptroller General of Patents; Case C-443/17. For the full text of this CJEU decision see ECLI identifier: ECLI:EU:C:2019:238; EUR-Lex - 62017CJ0443 - EN - EUR-Lex (europa.eu), CURIA - List of results (europa.eu)*

much in line with the CJEU's clear interpretation of the law as subsequently stated in *Santen* (see the operative part of that judgment and paragraph 51 therein). Thus, the definition of the product in Article 1 and Article 3 of the SPC regulation has to be construed strictly. In my view, approaching the MA in the present case as a document that authorises many products with effect from different dates goes contrary to this approach. Furthermore, the difference between these products (i.e., (i) the single product obinutuzumab; (ii) the combination product, obinutuzumab and bendamustine; and (iii) the combination product, obinutuzumab and chlorambucil) is based on their use and the therapeutic conditions they treat. However, this reassembles the approach based on 'relevant use' proposed by *Neurim* which the CJEU has recently decided is no longer the correct one (see discussion on *Santen* and *Neurim* below).

71 The applicant has argued that an SPC should be available to them for the combination because of the amount of research and testing necessary to gain approval for this combination from the relevant competent body in the UK (MHRA[20]). However, I note that the CJEU in *Novartis* C-442/11, was clear that an SPC provides patent-like infringement rights for a product, even when used in a combination, stating:

> *"Articles 4 and 5 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, where a 'product' consisting of an active ingredient was protected by a basic patent and the holder of that patent was able to rely on the protection conferred by that patent for that 'product'* ***in order to oppose the marketing of a medicinal product containing that active ingredient in combination with one or more other active ingredients, a supplementary protection certificate granted for that 'product' enables its holder, after the basic patent has expired, to oppose the marketing by a third party of a medicinal product containing that product for a use of the 'product',*** *as a medicinal product, which was authorised before that certificate expired."*

The implication I draw from this is that the SPC for the combination is not needed as well as the SPC for any of the single components as the latter will provide protection for a combination containing that component. Thus, the situation is not quite as the applicant characterises it, obtaining a combination SPC is not the only way to protect the combination.

72 I consider that this view is reinforced by the decision in *Santen* also. In paragraph 55 of the judgment, the CJEU made clear that not all research will result in an SPC (my emphasis in bold below):

> *"Thus, as is apparent from paragraph 11 of the Explanatory Memorandum referred to in paragraph 45 above,* ***the EU 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*** *(see, to that effect, judgment of*

[20] *Medical and Healthcare products Regulatory Authority*

21 March 2019, Abraxis Bioscience, C-443/17, EU:C:2019:238, paragraph 37).”

73 As noted earlier, the present SPC application is the third application by the applicant relying on the same marketing authorisation EU/1/14/937; although only one of the two earlier applications has proceeded to grant in the UK. The applicant considers that the additional clinical testing and related assessment required for the combination of obinutuzumab with bendamustine and, by implication, the combination of obinutuzumab with chlorambucil, warrants the marketing authorisation to be treated as in effect three separate marketing authorisations. The applicant suggests that this should be the case for a Type-II variation to the marketing authorisation, such as is the situation with the combination which is the subject of the present application. As I indicated above above, I see nothing in the *Medeva* and *Georgetown* decisions that causes me to regard the MA as authorising multiple medicinal products. I cannot find anything in the above-mentioned UK and CJEU court decisions that justifies one to take, what I consider to be a very large leap indeed, to arrive at the teleological interpretation proposed by the applicant.

74 By contrast, I consider that those illustrative passages picked out from the Commission Implementing Decision and the SmPC by the examiner (see earlier discussion above) provide an alternative, and, in my view, the correct and more consistent view, i.e., the product (or active ingredient) which is the subject of the marketing authorisation in this case is obinutuzumab alone. Indeed, this remains the case despite the type-II variation, and irrespective of what examples of the use of obinutuzumab in combination with other active ingredients are illustrated in the MA.

75 At this point, I think it is also relevant to note that, given the statement from *Novartis* quoted above, there already exists protection for the combination, albeit that this is patent-like infringement rights afforded to the applicant through the SPC already granted. This already granted SPC will provide protection for both the single product (obinutuzumab) and combinations including obinutuzumab (such as obinutuzumab and bendamustine). This is the only point of difference I see with the situation in the *Yeda* cases and the present case, as in the cases concerning Erbitux, the applicant had no prior SPC for the single product.

76 Returning to the relevance of *Yeda*, whilst I note the arguments made about the fairness of allowing an SPC for a loose combination, in the absence of any argument from the applicant that allows me to distinguish the facts of the present case from the *Yeda UK* decision, I do not believe I am in a position where those arguments allow me to disregard the specific finding of the High Court in *Yeda UK* with respect to the requirements of Article 3(b). The marketing authorisation the applicant is relying on is one that identifies a single active ingredient, albeit one with restrictions on its use; very much the situation considered by the High Court.

Conclusion

77 For the reasons given above, I conclude that the marketing authorisation provided in support of SPC application SPC/GB17/055, is not a valid authorisation to place the product, when defined as a combination of obinutuzumab and bendamustine, on the

market in the UK and thus this application does not meet the requirements of Article 3(b) of Regulation 469/2009.

78 Also I consider that the marketing authorisation provided in support of this SPC application relates to the product obinutuzumab alone and so can only be used in support of an SPC for the single product. However, such an SPC has already been granted to this applicant for this product. Consequently, I consider that the present SPC application does not satisfy Article 3(d) of Regulation 469/2009.

79 Therefore, SPC application SPC/GB17/055 is rejected under Article 10(2) of the SPC regulation for failure to meet the conditions laid down in Article 3 of this regulation.

Appeal

80 Any appeal must be lodged within 28 days after the date of this decision.

Dr L Cullen
Deputy Director, acting for the Comptroller