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The definition of product in the SPC Regulation: (Part 1 of 2) What's in a name?

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Farmitalia Carlo Erba Srl's SPC Application, Re (C-392/97) EU:C:1999:416; [1999] E.C.R. I-5553 (ECJ (5th Chamber))

Yeda Research and Development Co Ltd v Bureau voor de Industriele Eigendom (BIE) unreported (Netherlands)

Pharmaq AS v Intervet International BV (E-16/14) (EFTA)

Medeva BV v Comptroller General of Patents, Designs and Trade Marks (C-322/10) EU:C:2011:773; [2011] E.C.R. I-12051 (ECJ (4th Chamber))

***E.I.P.R. 555** *Anyone familiar with SPC law will know the importance of the definition of "product" for SPC purposes. "Product" is defined within art.1(b) of Regulation 469/2009 (the SPC Regulation) and plays a central role in the interpretation of that Regulation, in particular as regards the conditions for obtaining an SPC set out in art.3. This article examines how companies have approached the definition of product when applying for SPCs, how the understanding of this definition has developed since the SPC Regulation came into force, and how various courts within Europe (including the Court of Justice of the EU) have dealt with the definition of product. In addition, we provide some proposals for how the definition of product could be amended and a useful historical background to the definition of product in the SPC Regulation.*

Introduction

The EU Commission has recently decided to conduct a study into the legal aspects of Supplementary Protection Certificates (SPCs) and the UK has recently voted to leave the EU. Both of these circumstances make now an appropriate time to consider the current law as set out in the SPC Regulation.

In an earlier paper on (SPCs)[1] Dr Rollins discussed the diminution of the SPC term since SPCs were introduced in 1993. This article is Part 1 of a two-part series which looks in more detail at the current law governing SPCs. Part 1 is concerned with the definition of "product" in the SPC Regulation, whereas Part 2 will focus on SPCs covering combination products.

Anyone familiar with SPC law will know the importance of the definition of "product" for SPC purposes. "Product" is defined within art.1(b) of Regulation 469/2009 (the SPC Regulation) and plays a central role in the interpretation of that Regulation, in particular as regards the conditions for obtaining an SPC set out in art.3. This piece will examine how companies have approached the definition of product when applying for SPCs, how the understanding of this definition has developed since the SPC Regulation came into force and how various courts within Europe (including the Court of Justice of the EU (CJEU)) have dealt with the definition of product. In addition, we will provide some proposals for how the definition of product could be amended. A useful historical background to

the definition of product is also set out in the Annex.

The general understanding of the term "active ingredient" in practice

In our experience, innovative pharmaceutical companies consider the term "active ingredient" to mean, in the case of a small molecule, the pharmacologically active compound or substance of the medicinal product, i.e. the molecule that is responsible for the physiological or pharmacological action of the drug product in the patient and *not*, for example, the particular salt form in which the molecule is marketed. By way of illustration, the European Medicines Agency website[2] states under the entry "What is Resolor?" that "Resolor is a medicine that contains the active substance prucalopride", not "prucalopride succinate" (the form in which prucalopride is marketed). Similarly, for the entry "What is Januvia?" it states that "Januvia is a medicine that contains the active substance sitagliptin", not "sitagliptin phosphate monohydrate" the form that is marketed. This is because the salt/hydrate element of the substance does not change the substance's basic physiological effects.

This interpretation is consistent with the Definitions set out in the current version of Directive 2001/83 (as amended) which governs the regulation of medicinal products in Europe and is referred to frequently in practice during the drug development process. Although the Definitions section does not contain a definition of "product", the definition of "generic medical product" in art.10(2)(b) states that "different salts, esters … of an active substance shall be considered the same active substance, unless they differ significantly in properties …".

This is also consistent with the situation in the US. The US Code of Federal Regulations Title 21 Pt 314 provides a definition of active moiety and new chemical entity (ss.314.3 and 314.108, respectively):

"*Active moiety* is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other ***E.I.P.R. 556*** noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance.

New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act."

In reality, this is how pharmaceutical companies interpret the term "active ingredient", which is supported by the way that such companies approach the drafting of patent claims covering a new chemical entity (NCE) and how they often define the product (as set out in the "Product Description" of the SPC) when applying for an SPC (discussed in detail below). In line with this approach, our position is that a narrow interpretation of the definition of "active ingredient", which limits that definition to the particular marketed salt or, for example, the hydrated form of a salt of a new small molecule, is not an interpretation which should be applied in SPC law.

The standard approach to drafting patents on new chemical entities (NCEs)

It has always been common practice, for inventions relating to NCEs, to draft a patent application with a set of product claims that become progressively narrower, typically ending with a narrow general structural formula, a list of compounds identified by their chemical names or structures, or a specific chemical compound identified either by its name or structure. However, there are a number of reasons why a compound under development might not be the subject of a specific claim when the patent application is filed or even when the patent is granted. In patent drafting there was (and still is) always a balance between, on the one hand, building the patent specification around the lead compound and, on the other hand, disclosing important commercial information when the application is published. The patent application is usually published about 18 months after the priority date, but the lead compound may only be publicly identified several years after the priority date (e.g. when a generic name (INN) is applied for, clinical trial information on the compound is published or the company developing the compound publishes information linking the code number for the compound with its structure).

Competitor companies monitor patent applications in the fields they are interested in and will synthesise/study compounds that are of interest. Thus, there is an advantage in not identifying the lead compound at the outset in a patent application. That said, before the patent application is granted, it was (and still is) good practice to insert a claim to the preferred compound if this is known

at that time.

Further, the average development time for a new medicinal product to enter phase III trials is over six years from the date of patent filing, while the average patent application is granted by the EPO less than four years from the filing date (see, e.g., EPO Facts and Figures 2012, which stated that in 2011 the average grant was 44.3 months from filing[3]). The development of a putative medicinal product may not have progressed sufficiently to allow the lead compound to be selected, or the original lead compound may fail and a back-up not be selected during the time that the patent application is pending at the EPO. There is also the possibility that the lead compound may be covered by a general "Markush" formula but not subject to a specific disclosure in the patent.

Dr Rollins has examined the patents on the UK IPO register for the years 1994–2011[4] that relate to SPCs for new molecules.[5] About half of these SPCs relate to a drug approved in the form of a salt and just less than 10 per cent relate to a drug in solvated form (normally a hydrate). Of over 200 SPCs based on patents that relate to NCEs, between 25 and 33 per cent (reasonably evenly distributed over the 17-year time-frame) are based on patents that do not contain a claim to the specific chemical compound that forms the medicinal product. These patents either contain claims that have Markush formulae covering the specific chemical compound, or they contain claims to a list of compounds that includes the chemical compound. There are approximately equal numbers of patents where the specific chemical compound is claimed within a Markush formula to those where it is claimed in a list of compounds.

Salts and hydrated forms in patent drafting

Salts are prepared in the pharmaceutical development process to improve the properties of the active ingredient.

Commonly there are only one or two salts set out in the Examples of the basic patents (at most). As part of the above-mentioned research, Dr Rollins went through the Examples in the specifications of the basic patents that claimed salts of NCEs and on which SPCs between 1994 and 2011 are based. The combined numbers of such patents that contained no Examples or only one Example of a salt was almost 66 per cent of the total number of basic patents claiming salts. The number of patents where there are more than two salts exemplified is less than 20 per cent of the total. This lack of exemplification of salts is the case even where the claims of the patent on which the SPC is based relate to salt forms of the drug. For example, in the case of the EP 0,287,150 patent on ***E.I.P.R. 557*** rocuronium bromide upon which the SPC (SPC/GB94/009) is based, only the bromide salts are disclosed in the Examples.

Similarly, specific salts of drugs are only rarely claimed in the basic patents that relate to them; in the years 1999 to 2011, only between 25 and 33 per cent of the patents upon which an SPC was granted to a salt contained specific claims to that salt. It is not surprising that there is not a specific claim to the salt in the majority of cases even after high throughput screens for salts existed (which made the productions of salts easier); this is because whether to market the drug in unsalted or in salt form will be decided upon during the development process, and the specific salt chosen is often the subject of significant Research & Development effort after the patent has been granted.

The same applies to hydrates (and more generally solvates). In fact hydrates are only very rarely mentioned in claims of "basic salt" patents. Between 1993 and 2011, around 20 SPCs referred to the hydrate or solvate of a basic compound in their Product Description. Over 50 per cent of the basic patents for these SPCs did not claim hydrates/solvates. As with salts, this is not surprising as hydrates are usually investigated later during the development process. Indeed, the patent on the new molecule will often be granted before hydrates are investigated. An example of an SPC which relates to a hydrate is SPC/GB07/046, which relates to mometazone furoate monohydrate; however the hydrate is not claimed in the basic patent.[6]

Impact of patent drafting on SPC drafting

The practice of patent drafting described above inevitably impacts on the drafting of SPC applications. It was (and is) the practice when drafting SPC applications, and in particular the Product Description, to mirror as closely as possible the basic patent claims. In addition, the Product Description of the SPC may also attempt to mirror the precise form of the product in the MA as closely as possible.

Often therefore, if the product was marketed as a salt, the SPC would include the wording "compound X (optionally) in the form of a salt especially Y", where X is the compound and Y the specific marketed salt. Similarly, if the compound was marketed in the form of a hydrate, then the Product Description might include the wording "X Y Z hydrate" where X is the compound (which may be in the form of its salt Y) and Z reflects how many molecules of water compared with molecules of X; for example, monohydrate means a molar ratio of 1:1 and dihydrate means two molecules of water (hydrate) to one of the compound. An example of this is mometazone furoate monohydrate, referred to above.

The upshot of the above practices is, however, that a relatively inconsistent approach has been taken to the drafting of SPC Product Descriptions granted between 1994 and 2011. Indeed, for a product marketed in its salt form one may see simply "compound X" in the Product Description. Alternatively, one could see "compound X (optionally) in the form of a salt especially Y". For a product marketed in its hydrated form, one might see either of the above approaches or an additional third approach which includes the hydrated wording, such that the Product Description reads "compound X (optionally) in the form of a salt especially Y, most preferably X Y Z hydrate". In other words, while some SPC holders would include only the active ingredient in the Product Description, others would include a cascade, starting with the lead compound, then its salt and finally its marketed hydrated form.

The status of the Product Description

In our experience of defending the validity of SPCs in the UK, one is often confronted with invalidity arguments based on the wording set out in the SPC's Product Description. The basis of these arguments is, in effect, that the Product Description should be treated in the same way as a patent claim and should delineate the scope of the SPC. In other words, what the SPC holder writes in the Product Description box should be used as the definition of the "product" for the purposes of art.1(b) of the SPC Regulation. If the wording of that definition is broader than what is covered by the wording of the claims of the basic patent, then the product is not protected by the basic patent in force and the SPC therefore falls foul of art.3(a) of the SPC Regulation.

It is our view that this cannot be the correct way to approach the Product Description. Applying for an SPC was (and is) supposed to be a relatively simple and straightforward administrative exercise which requires only the filling out of a short form. Indeed, Mr Justice Arnold noted in his recent decision in *Sandoz v Searle* that the SPC system is supposed to be "a simple and transparent system".[7] The scope of an SPC is determined by art.4 of the SPC Regulation, which limits the scope to the active ingredient that is the subject of the relevant marketing authorisation. Nowhere does the SPC Regulation state that the scope of the SPC is to be determined by construing the Product Description like a patent claim. Opening up SPC holders to an additional invalidity attack based on the wording of the Product Description is therefore unjustified. ***E.I.P.R. 558***

Impact of a narrow definition of product on SPC practice for NCEs

What would be the effect of limiting SPCs, where the active ingredient is in the form of a salt, to the specific salt exemplified/claimed in the basic patent on which the SPC is based?

The physical form of a drug does not determine its inherent physiological activity. While the physical form may be important in terms of delivering the drug to the patient, it is the parent molecule cation (i.e. the active ingredient) that actually treats the patient's condition, not the salt anion. As generic companies are able to reference an innovative NCE product when applying for a generic MA, obtaining an MA on a different salt from that in the original MA is much more straightforward than applying for an MA from scratch. This is largely because the later MA application is primarily based on bioequivalence data between the two salts. This point is an extremely important one. What the regulator cares about is the active ingredient, and not normally the salt. If a company can show that the same active ingredient has the same effect in patients as an already authorised drug product, then approval will be granted much more quickly, even though the salt may be different.

Between 1999 and 2011, around 50 per cent of the "basic salt" SPCs (those where the basic patent claimed salts) granted in that period related to products marketed as salts and only about 12 per cent of the "basic salt" SPCs granted in that period were based on patents that claimed the specific marketed salt. Therefore, if SPCs were to be limited to the specific salts claimed in the patent, about 38 per cent of the "basic salt" SPCs filed between 1999 and 2011 would be invalid.

Further, if SPCs were to be limited to specifically claimed salts, generic companies would be able to design around the claims by developing new bioequivalent salt forms of the active ingredient. Thus, even the few SPCs that are based on patents that claim the specific salts would have little value unless the court were to hold there was infringement by equivalence. Indeed, it is precisely this issue that the CJEU sought to resolve in the *Farmitalia* case.[8] The CJEU decided in that case that generic companies should not be permitted to design around SPCs by the use of a different form of the same active ingredient. This decision is crucial to innovative pharmaceutical companies and, without it, generic companies would be able to readily avoid SPCs and thereby drive a coach and horses through the policy underlying the SPC Regulation. As explained further below, it is our view that the decision in *Farmitalia* remains good law and that its scope should not be limited based on later decisions of the CJEU (e.g. in *Medeva v Comptroller General (C-322/10)* [9]).

In addition, many of those products that are not marketed as salts but contain a suitable functional group, such as an amino group or a carboxy group, could probably be prepared in salt form. Just over 80 per cent of the patents on which SPCs are based on NCEs between 1994 and 2011 contain claims to the new molecule/chemical entities in salt form and presumably the applicants felt that salt forms of the NCEs could be prepared in these cases. If one argued (e.g. further to the CJEU's decision in *Medeva*) that the SPC is limited to the form of the drug that is identified/specified in the wording of the claims of the patent, then these SPCs on products not marketed as salts would presumably be held to be limited to the non-salted form unless the patent contained a claim to the specific salt (which is unlikely). Thus, again, even for the SPCs that relate to non-salted products, many would have little value unless the court were to hold that there was infringement by equivalence.[10] Consequently, the majority of chemical SPCs would have little value.

The return on investment for pharmaceutical companies is already under threat.[11] Further removing SPC protection for so many products would raise significant concern in practice. In addition, it would disincentivise innovative pharmaceutical companies from developing small molecules. This was not what the Commission intended or what the UK Patent Office or users had understood the purpose of the system to be when it was introduced.

How the courts have approached the definition of "product" in the SPC Regulation

From the late 1990s onwards, different European courts started to examine the definition of "product" under the SPC Regulation. The most notable of these cases at the time (and today), were the *Farmitalia case (C-392/97)* and the *Yeda* decision of the Netherlands Council of State. The former deals with small molecules, while the latter relates to biological products. This is an important distinction. Many of the CJEU's decisions on the level of specificity of the active ingredient required in the claims of the basic patent come from cases dealing with biologics. However, the CJEU has not limited the application of such judgments to biological products, even though the results of applying those judgments to small molecule SPCs can, from a policy perspective, seem perverse.

It is clear from the *Farmitalia* decision that the CJEU's view is that the definition of active ingredient (in analysing the scope of protection of the SPC) should be deemed to include any salts, esters or other derivatives of the active ingredient. That being so, the courts should not allow the requirement imposed by the later *Medeva* case (i.e. that the active ingredient be "specified or ***E.I.P.R. 559*** identified" in the wording of the claims) to be used to invalidate an SPC covering a small molecule product where the active ingredient is marketed in a specific salt or hydrated form but there is no claim to that specific salt or hydrate in the claims of the basic patent. To do so would be completely contrary to the policy underlying the SPC Regulation.

As regards biological products, the situation is different, as was made clear in the decision of the Dutch courts in the *Yeda* case. This case is discussed as follows in the *First Supplement of the CIPA Guide to the Patents Acts, 6th Edition (2010)* [12]:

"In *Yeda Research and Development Co Ltd v BIE, Case No. 200809060/1/H3*, the Netherlands Council of State rejected an application for an SPC in which the product was identified by the applicant as 'human monoclonal antibody against tumour necrosis factor-alpha' whereas the marketing authorisation identified the active ingredient as adalimumab. The applicant argued that a reasonable interpretation of *Farmitalia* implies that therapeutically equivalent variants of the product cited in the market authorisation may be included in the product description of a certificate to the extent that these are protected by the basic patent. Since the basic patent in question also protected other monoclonal antibodies which it may be assumed are therapeutically equivalent to adalimumab,

the applicant argued that the certificate should include a broader production description. Rejecting an appeal from the decision of the District Court of the Hague, the Council of State held that this case, involving a biological medicinal product, differed fundamentally from the situation in *Farmitalia* and that it cannot be assumed that the therapeutic value of the monoclonal antibodies against tumour necrosis factor-alpha related to adalimumab is in principle the same. At the UK-IPO it seems to be established practice that for macromolecules such as monoclonal antibodies, the product is defined in terms of the INN (International Non-Proprietary Name)."

Thus in *Yeda*, the Council of State distinguished small molecule cases, such as *Farmitalia*, with cases involving biological medicinal products, such as monoclonal antibodies (e.g. TNF).

The therapeutic equivalence of biological products has also been more recently considered in the decision of the EFTA Court in *Pharmaq v Intervet (Case 16/4)* in a referral from the Oslo District Court. The case concerned fish vaccines and the EFTA Court found as follows:

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> "It follows that the term "active ingredient", for the purposes of applying the SPC Regulation, concerns substances producing a pharmacological, immunological or metabolic action of their own.
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> …
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> 86
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> In that regard, the protection conferred on a medicinal product by an SPC may be relied upon in order to oppose the marketing of another medicinal product containing the same active ingredient with a therapeutic effect falling within the same therapeutic indication (compare, *mutatis mutandis*, *Forsgren*, cited above, paragraph 36 and case law cited). Otherwise, it would be possible for medicinal products which were, in principle, therapeutically equivalent to that protected by the SPC to compete with the latter. Such a result would frustrate the purpose of the SPC Regulation, which is to ensure the holder of the basic patent of exclusivity on the market during a given period extending beyond the period of validity of the basic patent (compare, to that effect, *Farmitalia*, cited above, paragraph 18).
>
> …
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> 89
>
> It follows from the considerations set out in paragraphs 81 to 87 of this judgment that the Defendant may prevent the Plaintiff from marketing its vaccine, provided it contains the same active ingredient with a therapeutic effect that falls within the therapeutic indications for which the Defendant's marketing authorisation and subsequent SPC has been granted." [13]

The Norwegian Court of Appeal subsequently commented in this case that:

"The [*Farmitalia*] judgment attaches importance to the purpose of the Regulation in establishing the concept of product for generic medicinal products, but in the Court of Appeal's opinion, the decision otherwise gives limited guidance for understanding the term 'the same active ingredient' used in biological medicinal products.

The decision in the '*Yeda* judgment' rendered by the *Dutch appellate court Raad van State (Judgment 200809060/l/H3), on 19 August 2009*, is, in the opinion of the Court of Appeal, more illustrative of the issue in our case.

…

The Court of Appeal's understanding of the [*Yeda*] judgment is that, in the context of a biological

medicinal product, as opposed to the *Farmitalia* case, there are not sufficient grounds to derogate ***E.I.P.R. 560*** from the description of the active substance described in the marketing authorisation. This is because even minor differences in the antibody could have significant effects on the quality, safety and efficacy of the medicine in question." [14]

The Norwegian Court of Appeal went on to say that it was unclear to them where the line should be drawn for a biological product to be seen as the same active ingredient. However, the court did state that the fact that the vaccine of Pharmaq (the alleged infringer) was "systematically, consistently and significantly more efficacious" meant that it could not be seen as the same active ingredient as the strain of virus marketed by Intervet.

Thus, the Norwegian Court of Appeal's clear view is that a slight change in the structure of an antibody can mean that it may not possess the same therapeutic value as a reference antibody. An analogous situation in the chemical field would be where a functional group of an active ingredient is changed, for example a carboxylic acid group being replaced with a different acidic group such as a tetrazole or a sulphonic acid group. Such modifications would not have been and would not be considered to be covered by the SPC, as they would result in a different compound with different physiological properties (if any). This is different from the position where the active ingredient takes the form of either a free compound or the form of a salt, ester or hydrate. In this situation, the form of the active ingredient does not impact on its physiological properties.

The impact of the *Medeva* decision

Following the *Farmitalia* decision, our experience was that the majority of practitioners considered that that the scope of "product" for small molecules under the SPC Regulation was settled, even if the precise scope of SPCs over biologics products remained (and still remains) somewhat unclear. However, as alluded to above, there is a residual concern that the *Medeva* line of decisions may have in some way altered the effect of the *Farmitalia* decision.

In *Medeva* the CJEU stated that:

"Regulation No 469/2009 must be interpreted as precluding the competent industrial property office of a Member State from granting a SPC relating to active ingredients which are not specified in the wording of the claims of the basic patent relied on in support of the SPC application." [15]

In the *University of Queensland* and *Daiichi* cases,[16] the CJEU reiterated this wording but referred to the active ingredients being identified rather than specified in the wording of the patent claims.

The result of this line of cases has been that those attacking the validity of an SPC now frequently claim that where the marketed salt or other (e.g. hydrated) form of the active ingredient is not specifically claimed in the basic patent, the SPC covering that active ingredient should be invalid. As mentioned above, our view is that, in single small molecule cases, parties should not be allowed to limit the definition of product to the specific salt so that they can then in turn then rely on *Medeva* to argue that the specific salt is not sufficiently specified in the claims of the basic patent.

Rather, the position should be that where the active ingredient is claimed (including within a Markush formula) in the basic patent, that should suffice on the basis that the definition of active ingredient for small molecules should be held to include any of its salt, ester or other derivative forms, such that the scope of protection of the SPC extends to those products. This should apply even where there is no claim to the specific marketed salt (or other) form in the basic patent. As the CJEU made clear in *Farmitalia*, and was reaffirmed most recently by the EFTA Court and the Norwegian Court of Appeal, if the rules were different it would be possible for medicinal products which are therapeutically equivalent to that protected by the SPC to compete with the latter. Such a result would frustrate the purpose of the SPC Regulation, which is to ensure the holder of the basic patent of exclusivity on the market during a given period extending beyond the period of validity of the basic patent.

In short, *Farmitalia* remains good law, and the rationale behind that judgment is still clearly applicable to small molecule cases. While some later decisions (such as *Medeva*) are arguably inconsistent with *Farmitalia*, they should not be allowed to limit its effect in small molecule cases. In this regard, the very recent decision of Arnold J in the English High Court in *Sandoz v Searle* is encouraging. In that case, Arnold J cited the CJEU's judgment in *Eli Lilly v HGS* [17] and found that it is sufficient for art.3(a) purposes for a basic patent's claim to specify an active ingredient by means of a Markush formula which covers it. In our view, this clear decision (from a judge with vast SPC experience) in support of

SPCs covering single active ingredients is very welcome.

How should single active ingredients be dealt with for art.3(a) SPC Regulation purposes?

The simplest definition of what constitutes "protected by" for art.3(a) purposes is "falls within the claims of the patent", i.e. an infringement test. This approach was ***E.I.P.R. 561** rejected in the UK by Jacob J in *Takeda*,[18] and has also been rejected by the CJEU.[19] However, the vast majority of the cases that consider what constitutes "a product protected by a patent" are combination cases. Indeed, the reluctance to adopt an infringement test appears to be almost solely based on concerns relating to combinations and, in particular, to parties being able to apply for SPCs covering numerous combinations of different known actives along with the active which is in fact the focus of the basic patent. This split between single and active ingredient cases was noted by Warren J in *Eli Lilly v HGS*,[20] where he distinguished between basic patents which relate to single active ingredients and those which relate to combinations:

"If the product falls within the claims, it will be protected within Article 3(a). This, however, has to be made subject to one proviso to which I turn.

The proviso relates to products which are combinations of active ingredients and is necessary to reflect the *Medeva* approach where the claims contain some general word or words extending their extent beyond the principal scope of the claims, typically by the use of a word such as ‘comprises’. In the absence of such an extending word, the claims have a focused scope and the question is simply whether the product falls within the scope of the claims. In the language of *Medeva* , the question is whether the product (ie the combination of active ingredients) is ‘specified’ in the claims, a question which is answered by a close examination of the claims. If general words are included, the position is different. The product does not fall within the focus of the claims and is not within its scope apart from the general words. In such a case, the product is not ‘specified’ any more than it is ‘specified’ where the general words are absent."

It is submitted that Warren J applied the correct test for single active ingredient products (which he notes "will give the same result as an infringement test in many cases") and that a distinction needs to be made between SPCs relating to single active ingredients and those relating to combinations. Thus, for SPCs relating to single active ingredients the correct approach is to apply an infringement test. The approach for combinations of active ingredients will be discussed in Part 2 of this series.

Proposals

As mentioned in the introduction, now is an appropriate time to consider the current law as set out in the SPC Regulation. The following proposals should therefore be considered:

1. "Active ingredient" in art.1(b) should be construed (or, if the SPC Regulation is to be amended, defined) in an analogous manner to "active moiety" in the US CFR Title 21 §314.3 (referred to above).

2. If the scope of protection provisions of the SPC Regulation (e.g. art.4) are to be revised, then *Farmitalia* should be codified, i.e. it should be made clear in the SPC Regulation that in small molecule cases protection of the SPC extends to any derivative forms of the active ingredient, irrespective of whether such forms are expressly specified/identified in the wording of the claims.

3. For single active ingredient claims, the question that should be asked in order to determine if a product is "protected by a basic patent" in art.3(a) should be whether

the product in question falls within the scope of the claims of the basic patent, without anything more being required. We note that Switzerland applies the infringement test in SPC cases and that the UK could also consider adopting such a position post-Brexit to encourage further R & D investment in the UK by pharmaceutical companies (even if the EU takes a different approach).

Annex: Historical background to the definition of "product"

In January 1993, SPCs took effect as a new IP right in the UK (and elsewhere within the Community), pursuant to the SPC Regulation. SPCs were to be granted by the national patent offices under the conditions and having the effects laid down in Regulation 1768/82 (what later became the SPC Regulation). The rationale behind the introduction of the SPC Regulation is set out in the Commission's Explanatory Memorandum dated 11 April 1990.

The definition of "product"

Article 1(b) of the SPC Regulation defines "product" as "the active ingredient or combination active ingredients of a medicinal product". The term "active ingredient" is not defined in the SPC regulation. This lack of definition has caused significant problems as the case law on the SPCs has developed in national courts and the CJEU. ***E.I.P.R. 562***

The development of the meaning of "product" in SPC practice

Prior to the SPC Regulation coming into force, two articles were published on the proposed regulation by the English solicitors Robin Whaite and Nigel Jones in the E.I.P.R. in 1990 and 1992.[21]

In the 1992 article, in the section headed "Scope of Protection", the authors considered whether or not the "product" is the specific product for which marketing authorisation has been granted (for example, the acid form of a compound), or whether it extended to other chemical forms of that product (for example to salts and esters of the acid). Whaite and Jones explained that the Annex to the Common Position text of the Regulation agreed at the Council meeting on 19 December 1991 was "an apparent attempt" to give some guidance on the issue. They also referred to Article 4 of the SPC Regulation. In light of these documents, they concluded that

"While several interpretations of this definition appear possible, the most appropriate appears to be that protection will be conferred on the active ingredient, however formulated, and for any therapeutic use covered by a marketing authorisation granted before expiry of the certificate".[22]

Although this was the authors' view, this position was later adopted by the UK Patent Office (as explained below).

When the SPC Regulation was introduced there was some guidance from the UK Patent Office in the form of its booklet *"Supplementary Protection Certificates for Medicinal Products: A Guide for Applicants" (the Patent Office Guide) published in 1992*. Although the introduction states that it was "intended to serve as a guide only and is not an authoritative statement of the law on Supplementary Protection Certificates", it was widely regarded as being a good guide to how the UK Patent Office would approach SPC applications and SPC practice generally.

At para.1.6, the *Patent Office Guide* stated that

"the term *'active ingredient'* will generally be interpreted as including any closely related derivative, in particular a salt or ester, which has obtained an authorisation to be placed on the market and is protected by the basic patent unless the derivative in question can be regarded as a new active ingredient".

It is our understanding that this is also consistent with the interpretation of the definition of "product" in the French CCP legislation that predated the European SPC legislation.

The Fourth Edition, Fourth Supplement of the CIPA Guide, published in 1993, contained a section

entitled *"Definition of product for which a supplementary protection certificate can be granted" (pp.339–340)*. This refers to discussion at the European Community Council to the effect that "product may cover salts and esters of the active ingredient". It also refers to the two articles by Whaite and Jones and the *Patent Office Guide*, as referred to above.

The Fourth Edition, Fifth Supplement of the CIPA Guide, published in 1995, repeated the section contained in the 1993 edition but added the observation that "a more stringent line has been taken in other countries and decisions of the courts can be expected". This referred to the fact that different countries were interpreting the definition of a "product" differently. This was important as there was a risk either that the scope of protection of SPCs might be interpreted differently by different countries or, if the matter was referred to the CJEU, then that court might adopt a narrow interpretation. Either of these alternatives would considerably diminish the value of SPCs. The minute of a meeting of national experts called by the European Commission that took place on 3 February 1995 explains this difference in the interpretation of the "product" as follows:

"Several delegations concurred with this interpretation, which was consistent with joint applications of Article 1(b) and 4 of the Regulation. In their view, all pharmaceutical derivatives of a given substance were in general covered by the certificate.

On this particular point two delegations advanced a different view. Namely that the protection provided by the certificate must be confined to the substance appearing in the marketing authorization; in support of their view, they relied on the ninth recital to the Regulation. Accordingly, if the marketing authorization covered a particular salt of a given base, the certificate protected only that salt and not the base or its other pharmaceutical derivatives."

The Netherlands was one of the two countries taking the more stringent view. However, following the 1995 meeting, the Dutch Patent Office subsequently changed its position, with the result that it allowed the "product" to be defined as the parent molecule, optionally in the form of a salt. This interpretation had earlier been echoed in a decision from the Appeal Department of the Dutch Patent Office on 24 January 1994 regarding an antidepressant drug, paroxetine, which was discussed in the following terms in an article by John N. Adams[23]:

"The relevant marketing authorisation stated that the product contained paroxetine hydrochloride hemihydrate, equivalent to 20 mg of paroxetine. The ***E.I.P.R. 563*** Merck Index in the entry for paroxetine describes paroxetine hydrochloride and paroxetine maleate in addition the hemihydrate. The court concluded:

‘Whatever the form in which it appears, for example salt, whether hydrated or otherwise, paroxetine is the active principal and must be taken as the product within the meanings of Articles 1 and 3 of the Regulation.’

A problem here is the term ‘active principal’, which does not appear in the Regulation, but presumably, given the vagaries of translation, what is meant is ‘active ingredient’. In fact, at first instance, where the point under discussion was actually decided (it was not in issue before the court) the Examiner had concluded:

‘In pharmaceutical literature no potential distinction is made between paroxetine, the hydrochloride or the hydrochloride hemihydrate thereof, although there will be chemical, physical and biological differences, that with regard to "Seroxat", *the Special Department will not consider the designation "active ingredient" as referred to in Article 3(a) and (b) according to Article 1(b) in a way other than is conventional in pharmaceutics, because the Regulation is drawn up for the benefit of the pharmaceutical industry so that "Seroxat" paroxetine is regarded as the active ingredient, as has been explained in the preceding consideration by reference to publication*.’(emphasis added)

This, it is submitted, precisely hits the nail on the head."

What did companies think about the product definition when the SPC Regulation was introduced in 1993 and how did practice change as a result of Patent Office practice?

When the SPC Regulation came into force, Dr Rollins was in the patent department of the pharmaceutical company The Wellcome Foundation Ltd (Wellcome). The team there discussed the advent of the system within the patent department and how they should operate under it. Following these discussions, Wellcome developed a policy of giving the trade name as the definition of the

"product" when completing the SPC application form published by the UK Patent Office, as the trade name was what was given as the name of the product in the MA. Wellcome's view was that alternative forms of the active ingredient (e.g. salts, simple esters, hydrates, etc.) would be covered by the SPC when the trade name was specified. The basis for this belief was the Guidance issued by the Patent Office and the articles by Whaite and Jones discussed above.

Dr Rollins has obtained the files for four SPCs that Wellcome filed in 1993 (SPC/GB93/032, 040, 042 and 058). In these, the trade name was specified as the "product". However, the Patent Office argued that the reference to the product by its trade name was not clear. Thus, in the case of SPC/GB93/058 the definition was changed in November 1993 from its trade name, LAMICTAL RTM to lamotrigine (the generic name/INN) "optionally in the form of an addition salt with a pharmaceutically acceptable acid".

Other large pharmaceutical companies who filed SPC applications immediately after the Regulation was introduced early in 1993 also had narrow definitions of the product, even though the corresponding basic patents provided the basis for language in the form of "pharmaceutically acceptable salts thereof" or "optionally in the form of a pharmaceutically acceptable salt" (or equivalent language) to be included in the SPC. For example, Merck & Co Inc filed SPCs GB93/002, 003, 005 and 006, all of which had the trade name as the product in the SPC application. This was replaced in all cases and, in the case of SPC/GB/93/002 and 003 (where the product was marketed as a salt), the generic name plus "optionally in the form of …" language was added.

In relation to SPCs filed up to the end of May 1993 (on what appear to be NCEs) there seems to have been an approximately even split between those who restricted themselves in the SPC product definition to the specific salt or compound that was marketed and those who used the broader language referred to above. Of the latter group, at least some started off with narrower language but broadened the language in prosecution. However, looking at the large number of SPCs filed in June 1993 on NCEs, there is a 2:1 split in favour of the use of the broader language. By the time Dr Rollins's group filed an SPC application on an NCE in January 1995, Wellcome was using broader language covering salts as well as the parent molecule (even though the product was not marketed as a salt) and by, for example, 2002, there were very few SPC applications on NCEs that only claimed the specific compounds that were marketed (in fact in 2002 there were none).

In 2011, the last year we have studied, there were only two SPCs on NCEs where the product definition did not contain wording along the lines of "and pharmaceutically acceptable salts" or "or a pharmaceutically acceptable salt thereof" or similar language. One of these two SPCs (SPC/GB11/001) is based on a patent that claims only vinflunine ditartrate where the broader language was not appropriate and the product definition of the other concerns "17-substituted steroids useful in cancer therapy". This is a very unusual definition as it is extremely broad. Thus wording along the lines of "and pharmaceutically acceptable salts" or "or a pharmaceutically acceptable salt thereof" or similar language is still used extensively. In 2011, wording along the lines of "especially in the form of salt X" was also still being used (see for example SPC/GB11/031: ***E.I.P.R. 564*** tapentadol in the form of its base or a salt of a physiologically compatible acid, especially the hydrochloride salt).

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1. Rollins, "How Europe's SPC regime works in practice" (2016) 260 M.I.P. 54.

2. See http://www.ema.europa.eu [Accessed 23 June 2017].

3. This is, to our knowledge, the last year that the average grant time from filing was provided by the EPO.

4. 1993 was not included because this was the first year of operation of the SPC Regulation and transitional provisions were in place that could cause distortions for this year. 2012 and onwards were not included because there were still a large number of pending SPC applications for these years at the time that the work was carried out.

5. In performing this analysis it was necessary for Dr Rollins to exclude various types of SPCs on the register. As a first step, he ruled out of consideration SPCs that relate to agrochemical, veterinary or imaging agents and also SPCs that have not yet been granted, or have been rejected or withdrawn. He then excluded biological/peptide SPCs or SPCs that relate to uses/processes, etc., and selection inventions that relate to salts and/or hydrates where these are not salts and/or hydrates of a new molecule.

6. As a note, there are a number of examples where hydrates are claimed in specific improvement/selection patents—for example EP 0,548,114 (SPC/GB97/064), which relates to mometasone furoate monohydrate. However, we are not suggesting that this should be required for obtaining an SPC over a hydrated form of an active ingredient. In fact, we are suggesting quite the opposite.

7. *Sandoz Ltd v GD Searle LLC [2017] EWHC 987 (Pat)* at [67].

8. *Farmitalia Carlo Erba Srl (C-392/97) EU:C:1999:416; [2000] 2 C.M.L.R. 253*.

9. *Medeva BV v Comptroller General of Patents, Designs and Trade Marks (C-322/10) EU:C:2011:773; [2012] R.P.C. 25*.

10. For recent consideration of infringement by equivalence in the UK, see the Supreme Court case of *Actavis and others v Eli Lilly and Company [2017] UKSC 48*. The effect that this decision will have on the application of SPC law in the UK is a very interesting issue (though unfortunately outside the scope of this article).

11. Rollins, "How Europe's SPC regime works in practice" (2016) 260 M.I.P. 54.

12. *First Supplement of the CIPA Guide to the Patents Acts 6th Edition (2010), p.101*.

13. *Pharmaq AS v Intervet International BV (E-16/4) EFTA Court, 9 April 2015* at [84], [86], [89].

14. *Pharmaq AS v Intervet International BV, Borgarting Court of Appeal, Norway, 19 December 2016*.

15. *Medeva BV v Comptroller General of Patents, Designs and Trade Marks (C-322/10) EU:C:2011:773; [2012] R.P.C. 25* at [42].

16. *University of Queensland v Comptroller General of Patents, Designs and Trade Marks (C-630/10) EU:C:2011:780*; *Daiichi Sankyo Co. Ltd and Sanofi-Aventis Deutschland GmbH v v DEMO Anonimos Viomikhaniki kai Emporiki Etairia Farmakon (C-414/11) EU:C:2013:520*.

17. *Eli Lilly v Human Genome Sciences Inc (HGS) (C-493/12) EU:C:2013:835; [2014] R.P.C. 21*. Here, the CJEU found that, in principle, an antibody could be "protected by" a functionally defined antibody claim, even where the structure of the marketed antibody was not disclosed in the patent.

18. *Takeda Chemical Industries Ltd v Comptroller General of the Patent Office [2003] EWHC 649 (Pat); [2004] R.P.C. 3*.

19. See, for example, *Eli Lilly v HGS (C-493/12) EU:C:2013:835; [2014] R.P.C. 21* at [33].

20. *Eli Lilly v Human Genome Sciences [2014] EWHC 2404 (Pat); [2015] R.P.C. 8* at [65], [66].

21. Robin Whaite and Nigel Jones, "Pharmaceutical Patent Term Restoration: The European Commission's Regulation" (1990) 12 E.I.P.R. 179; Robin Whaite and Nigel Jones, "Pharmaceutical Patent Term Restoration: The European Commission's Regulation" (1992) 14 E.I.P.R. 324.

22. Whaite and Jones, "Pharmaceutical Patent Term Restoration" (1992) 14 E.I.P.R. 324, 325.

23. John N. Adams, "Supplementary protection certificates: the 'salt' problem" (1995) 17 E.I.P.R. 277.