Review of UKIPO SPC Decisions in 2022

In this review we examine decisions relating to SPCs issued in 2022 by the UKIPO's hearing officer and discuss the potential consequences for rights holders.

The decisions cover a range of different SPC provisions, and provide some clarity on the UKIPO's position on the interpretation of Article 3(d) of the SPC regulation following the UK's exit from the European Union, as well as new guidance on how to answer the fundamental question of "what is an active ingredient?" Arguably the most timely decision, though, relates to SPC applications for combination therapy products, as this topic is currently the subject of pending referrals before the CJEU, and the UKIPO has offered an interesting new perspective on the relevant provisions and case law governing such applications.

O/242/22: The application of Article 3(d) in the UK following Santen

Article 3(d) of the SPC Regulation requires that an SPC be based on the first authorisation to place a drug on the market as a medicinal product (the earliest marketing authorisation). The proper identification of the earliest marketing authorisation may be an issue when a patent protecting a second or subsequent medical use of a particular drug is used as the basis for an SPC application.

On 9 July 2020, the CJEU issued its landmark judgment in the Santen C-673/18 case (discussed in detail in our briefing note here), in which the court concluded that

*"Article 3(d) … 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."*

The Santen decision therefore effectively prohibits SPCs being granted in the EU based on a marketing authorisation to a new medical use or new formulation of an active ingredient (or combination of active ingredients) that has previously been authorised for other therapeutic applications. This decision explicitly overturned the earlier Neurim C-130/11 decision.

In proceedings before the UKIPO leading to a hearing officer decision in O/242/22 (*Janssen Biotech*), the precedent effect of the Santen decision in the UK, following the UK's exit from the European Union, was put to the test.

The SPC application leading to this decision was directed to the antibody product golimumab. Golimumab was first authorised in 2009 for the treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, and Janssen had obtained a first SPC to golimumab based on that marketing authorisation. Subsequently, a Type II variation of the marketing authorisation was granted, authorising golimumab for treatment of ulcerative colitis. Janssen then applied for a further SPC based on that later marketing authorisation.

The UKIPO examiner refused the application on grounds that, following Santen, the Type II marketing authorisation on which it was based was not the "first" marketing authorisation for golimumab within the meaning of Article 3(d). The case was therefore referred to a hearing officer.

At the hearing, the applicant argued that old UK case law should prevail over the CJEU's decision in Santen. In particular, it was argued that the England and Wales Court of Appeal judgment in *Neurim Pharmaceuticals v The Comptroller General of Patents* (full text available here) ought to prove decisive. Not only was this was the case that had led to the CJEU Neurim C-130/11 decision on Article 3(d), allowing SPCs to be granted based on second or subsequent marketing authorisations in certain circumstances, but the Court of Appeal had been strongly in favour of the approach that was ultimately adopted by the CJEU. Thus, went the argument, that because a higher court of England and Wales had explicitly sanctioned this more lenient interpretation of Article 3(d), this is the interpretation that should prevail in the UK now that the UK was no longer a member of the European Union or subject to the jurisdiction of the CJEU.

The hearing officer however noted that the CJEU's decision in Santen was passed down before the end of the Brexit "transition period" as set out in the EU Withdrawal Act, which ended on 31 December 2020. Thus, the Santen decision formed part of the body of EU case law that became part of UK domestic law after this date, and only the UK Supreme Court and England & Wales Court of Appeal have the power to depart from retained EU case law. Moreover, the hearing officer noted that the grand chamber of the CJEU (i.e. all 15 CJEU judges) sat in the Santen case, and Santen represents the only example in SPC case law of the CJEU explicitly overturning one of its earlier decisions. The hearing officer's view was therefore that the Santen decision must be treated as authoritative on the interpretation of Article 3(d), and any earlier case law from the UK courts decided prior to Santen was not persuasive.

The conclusion in this decision is unsurprising, given the generally accepted premise that EU case law decided up to 31 December 2020 would be applied by (at least) the lower courts in the UK. However, it does provide clarification on the UKIPO's approach to the interpretation of Article 3(d), and confirms that SPCs are indeed not available in the UK based on second or subsequent marketing authorisations of an already-authorised medicinal product – at least until this point is tested in a case that comes before the Court of Appeal or Supreme Court.

O/136/22: What evidence is admissible to demonstrate a substance is an "active ingredient"?

Another key decision issued in 2022 by the UKIPO is O/136/22 (*Ethicon/Omrix*) concerning the question "what is an active ingredient"?

Article 1(b) of the SPC Regulation requires that a "product" protected by an SPC must be

"an active ingredient or combination of active ingredients of a medicinal product."

This raises the questions of how far the definition of "active" ingredient extends, and what evidence applicants are able to advance to support an assertion that a particular component of a medicament is an "active" ingredient.

Case O/136/22 concerned an application for an SPC to *"thrombin, fibrinogen and oxidised regenerated cellulose (ORC)"* based on a marketing authorisation to the product EVARREST®. The dispute concerned whether ORC was an "active ingredient" within the meaning of Article 1(b) of the SPC regulation. This was critical to the outcome of the application, because there had previously been a marketing authorisation to the two-way combination of thrombin and fibrinogen as active ingredients. Thus, if ORC could not be considered an "active" ingredient, the SPC application would not have been based on the "first" marketing authorisation to the combination of (remaining) active ingredients thrombin and fibrinogen, and must therefore be refused under Article 3(d) of the SPC Regulation (following the CJEU decision in Santen, discussed above).

The UKIPO examiner refused the application on the basis that neither the Summary of Medicinal Product Characteristics (SmPC) nor the European Public Assessment Report (EPAR) for EVARREST® indicated that ORC had any pharmacological activity. The applicants, however, submitted that further documents did demonstrate that ORC had pharmacological activity, and that this evidence should be taken into account. The hearing officer therefore had to decide whether such further documents could be admitted in analysing whether ORC constituted an "active" ingredient.

In his decision, the hearing officer noted that the SmPC forms an integral part of an SPC application, with Article 8(1) (b) of the SPC regulation explicitly requiring that it be provided on filing of an SPC application. It is accordingly difficult to square an argument that content of the SmPC should be completely disregarded when determining what the "active ingredient" of a product is.

The applicants had referred in particular to the Forsgren C-681/13 decision of the CJEU as justification for their approach. In that case, the CJEU had ruled that a substance is an "active ingredient" under Article 1(b)

"only if it is established that it produces a pharmacological, immunological or metabolic action ***of its own … in light of all the facts*** *of the dispute in the main proceedings*"

However, the hearing officer noted that in Forsgren, there was at least some indication in the relevant SmPC that the substance in question (Protein D) *might* have pharmacological activity "of its own" (the SmPC in question showed that a particular antigen conjugated to Protein D had a certain activity that was absent from the corresponding unconjugated antigen). The hearing officer considered that it was on this basis that the CJEU considered it proper to evaluate the further evidence relating to the activity of Protein D under an "all the facts" analysis (which did ultimately show that Protein D had activity of its own).

The hearing officer considered this situation factually distinct from one where the SmPC/EPAR does not give **any** indication as to pharmacological, immunological or metabolic action of an ingredient, as in the present case. Further reference was also made to the UK High Court decision in *Abraxis Bioscience v The Comptroller General of Patents* (full text available here), in which the Court concluded that

"when considering whether a substance … constitute[s] an active ingredient, it is proper to refer to both the SmPC forming part of, and the EPAR…"

The hearing officer concluded that by parity of reasoning, it would be "improper" **not** to support the analysis with reference to the SmPC/EPAR. On the basis of this analysis, the hearing officer did not allow consideration of the further evidence relating to ORC, and refused the SPC application under Article 3(d).

Ultimately, the analysis of whether an ingredient within a medicament constitutes an "active" ingredient within the meaning of the SPC regulation will be specific to the facts of a given case. However, what this decision clarifies is that – in the UK at least – the correct approach to conducting that analysis can be summarised as an "SmPC/EPAR-led" approach, rather than an "SmPC/EPAR-only" or an "SmPC/EPAR-exclusionary" approach. Thus, if there is *at least some* indication of activity of the relevant ingredient in the SmPC or EPAR, it ought to be possible for an applicant of an SPC to later furnish further evidence confirming that the relevant ingredient does possess a requisite level of pharmacological activity to be considered an "active" ingredient of an authorised medicinal product.

O/711/22: A new UK perspective on Combi-SPCs?

"Combi-SPCs", i.e. SPCs directed to combination therapy products, are currently a hot topic in SPC law. In the past year, the Finnish and Irish courts have referred questions to the CJEU regarding the allowability of SPC applications to such products (see our news items on these referrals here and here for more detail), and the Swedish courts are now expected to follow suit (discussed in our news item here).

Those particular referrals relate to issues arising under Articles 3(a) and 3(c) of the SPC regulation in respect of combination products.

A recent UKIPO decision, O/711/22 (*Roche Glycart*), however presents a new perspective on combi-SPCs which also brings Articles 3(b) and 3(d) into play. Article 3(b) in particular requires that an SPC application be based on a valid authorisation to place "the product" on the market as a medicinal product.

The case at issue concerned an SPC application to the combination of obinutuzumab and bendamustine, based on a Type II variation of the marketing authorisation for GAZYVARO® (obinutuzumab). In this Type II variation, the clinical particulars of the SmPC for GAZYVARO® were updated to refer to use of GAZYVARO® in combination with bendamustine for treating follicular lymphoma. The Type II variation did **not**, however, include any update to the definition of the authorised product (in either the European Commission implementing decision, or the SmPC itself), which remained "obinutuzumab". The combination product itself was marketed as a so-called "loose" combination; in other words, the

two active ingredients were not formulated together (as in a "fixed" combination product), but rather were formulated separately and could be administered either together or with a time interval between administrations.

The key question to be answered in this case was, therefore, does the Type II variation of the marketing authorisation place "the combination product" on the market in the sense of Article 3(b)?

The applicant argued that it did, with specific reference to the CJEU decision in the joined cases of Medeva C-322/10 and Georgetown C-422/10. In Medeva/Georgetown, the CJEU ruled that it was possible to base an SPC to ingredient X on a marketing authorisation to combination product X+Y. If not, the law would unfairly prejudice manufacturers who are obliged, for legal or practical reasons, to market an active as a combination product. The applicant argued that the present case merely represented the reverse situation – basing an SPC to product X+Y on a marketing authorisation to X only – which must be allowable for similar reasons as presented in Medeva/Georgetown. In particular, it was argued that some manufacturers are unable to prepare a "fixed" combination product and instead must seek authorisation for a "loose" combination (e.g. where one component must be orally administered and another intravenously), and that such practical constraints should not preclude the manufacturer from obtaining an SPC. It was asserted, without evidence, that it can be just as difficult and expensive to develop these "loose" combination products as "fixed" combination products.

The hearing officer disagreed. In particular, a distinction was seen with the facts of Medeva/Georgetown case, because in Medeva/Georgetown both components of the combination were explicitly listed as active ingredients of "the product" in the SmPC (i.e. Medeva/Georgetown was only concerned with a "fixed" combination product). In the present case, however, the marketing authorisation was considered to be an authorisation of the **single** product obinutuzumab, that discusses different ways in which that product *might* be used in therapy in the "clinical particulars" section of the SmPC. According to the hearing officer, that is not the same as an explicit authorisation of a combination therapy product – or, in other words, the SmPC simply does not contain the level of information about bendamustine required to place the combination therapy on the market.

This point of view was underlined by the fact that one alternative possible use of obinutuzumab set out in the "clinical particulars" section of the SmPC was its use in chemotherapy. Without any further details, the hearing officer considered it clear that the marketing authorisation could not rise to the level of placing obinutuzumab and any chemotherapeutic agent on the market as a combination therapy product; thus, by parity of reasoning, the same conclusion must apply to the combination of obinutuzumab and bendamustine.

The conclusion of the hearing officer in this regard is also consistent with the England & Wales High Court in *Yeda v Comptroller General of Patents* (full text available here), which predates the Medeva/Georgetown decision but addresses a similar fact pattern to the present application.

Furthermore, as the Type II marketing authorisation could only be considered as a "new authorised use" of the single active agent obinutuzumab, this was also not the "first" authorisation to place obinutuzumab on the market, and therefore the SPC application was also refused under Article 3(d) (following the CJEU decision in Santen, discussed above).

The take-home message here for rights holders is therefore that it does, unfortunately, appear to be becoming increasingly more difficult to secure Combi-SPCs. In addition to challenges regarding the required level of disclosure in the basic patent (the subject of the pending CJEU referrals from the Finnish and Irish courts, and the likely further referral from the Swedish court), rights holders must also be careful to ensure that any marketing authorisation on which an application to a Combi-SPC is based rises to the required level of detail to place that combination product on the market. A mere reference to both active ingredients in the SmPC is unlikely to satisfy the requirements of Article 3(b) of the SPC regulation: rather, an explicit indication that both substances form the authorised "product" appears to be required. This may make it particularly challenging to secure SPCs to so-called "loose" combination products, in which two medicinal products are formulated and administered separately, as such products are likely to be the subject of two separate marketing authorisations (rather than a single marketing authorisation, as in the case of "fixed" combination products).

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