# CJEU Overturns Neurim – no SPCs for New Therapeutic uses of Old Active Ingredients

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.

Historically it had been thought that a patent to a new medical use of a drug could form the basis of an SPC, but that SPC had to be based on the earliest marketing authorisation for that drug, even if the earliest authorisation was for a different disease or condition from that specified in the patent. In practice, reference to the earliest marketing authorisation often meant that any resultant SPC would have a zero term, because of the maximum SPC term of 15 years from first marketing authorisation in the EU.

However, in the landmark Neurim decision, the CJEU indicated that under certain circumstances it is possible to base an SPC application on an authorisation which is not the first marketing authorisation to place a particular drug on the market. Specifically, the CJEU held in Neurim that the "first" authorisation for the purposes of Article 3(d) is the "first" authorisation "which comes within the limits of the protection conferred by the basic patent". That is, an earlier authorisation which is outside the scope of the basic patent should not be taken into account.

Following Neurim, there was much debate over how broadly the principles outlined in Neurim should be applied, with the various national patent offices diverging to a significant extent. For example, some offices applied Neurim very narrowly, such that an SPC was only granted if the earlier authorisation was veterinary and the later authorisation was for a different indication in humans (following the fact pattern in Neurim). Many offices applied a broader interpretation, such that SPCs were granted provided that the later authorisation was for any different therapeutic indication. However, some offices applied Neurim very broadly, such that SPCs were granted if the later authorisation differed from the earlier in any way, including e.g. the formulation of the active ingredient, the administration or dosage regime, or the specific patient population to be treated. The divergence in practice across Europe resulted in two referrals to the CJEU.

The first of these referrals was the Abraxis C-443/17 case. In summary, the CJEU held in Abraxis that SPCs are not available for new formulations of old active ingredients, but did not go as far as overturning Neurim (despite that being the recommendation of the Advocate General in his earlier opinion). Whilst the CJEU's conclusions regarding the unavailability of SPCs for new formulations of old active ingredients was not popular with innovator companies, there was relief at the time that the CJEU did not overturn Neurim.

The second of these referrals was the Santen case. Santen had applied for a French SPC based on a 19 March 2015 marketing authorisation for treating severe keratitis with ciclosporin. However, ciclosporin was the subject of an earlier marketing authorisation, dated 23 December 1983, for preventing the rejection of solid organ and bone marrow grafts and for other therapeutic indications, including the treatment of endogenous uveitis, an inflammation of all or part of the uvea, the middle part of the eyeball.

The French Patent Office (INPI) rejected the SPC, on the basis that the 19 March 2015 marketing authorisation was not the first marketing authorisation for ciclosporin, and thus that the requirements of Article 3(d) were not met. Santen appealed the rejection, arguing that the first marketing authorisation falling within the scope of the claims of the basic patent was the 19 March 2015 marketing authorisation, and thus, according to Neurim, an SPC should be granted. The Court of Appeal, Paris subsequently referred to the CJEU a series of questions regarding how Neurim should be interpreted, which are recited in paragraph 23 of the decision. Ultimately, however, the CJEU did not need to answer these questions, because it decided instead to overturn the Neurim reasoning entirely.

In overturning Neurim, the CJEU relied heavily (as it did in Abraxis) upon a strict interpretation of Article 1(b) of the SPC Regulation, which states that "product" means the active ingredient or combination of active ingredients of a medicinal product. In particular, the CJEU concluded (see paragraph 47 of the decision) that:

*"Article 1(b) of Regulation No 469/2009 must be interpreted as meaning that the fact that an active ingredient, or a combination of active ingredients, is used for the purposes of a new therapeutic application does not confer on it the status of a distinct product where the same active ingredient, or the same combination of active ingredients, has been used for the purposes of a different, already known, therapeutic application."*

The CJEU then went on to consider how Article 3(d) should be applied in view of this strict interpretation of Article 1(b), and held in paragraph 53 that *"contrary to what the Court held in paragraph 27 of the judgment in Neurim, to define the concept of 'first [MA for the product] as a medicinal product' for the purpose of Article 3(d) of Regulation No 469/2009, there is no need to take into account the limits of the protection of the basic patent".*

In view of these conclusions, the CJEU answered the various questions posed by the Court of Appeal as follows:

*"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."*

The CJEU's decision in Santen is likely to be controversial and unpopular with innovator companies. Not only does it mean that SPCs will no longer be available for new therapeutic uses of old active substances, but also previously-granted SPCs for new therapeutic uses of old active substances will be highly vulnerable to attack by generic competitors. In this regard, it is noteworthy that the CJEU has not provided any basis for a "transition" from the old interpretation of Article 3(d) of the SPC regulation (as per Neurim) to the new interpretation (as per Abraxis and Santen).

More generally, the Santen case represents the latest in a series of decisions from the CJEU that weaken the protection SPCs can provide for medicinal products. In particular, the CJEU has been using Article 3(a) of the SPC regulation to favour late-stage, clinical research into a specific product, and does not seem to recognise value in also incentivising broader, early-stage research. By contrast, the CJEU has now used Article 3(d) to remove an incentive to conduct particular forms of late-stage, clinical research into new uses of known compounds.

Although the CJEU considers that its reinterpretation of the meaning of Article 3(d) provides a "fair balance" between the needs of innovator companies and EU legislature's intention to take into account "all the interests at stake" (see paragraph 55 to 57), in doing so it appears to have disregarded the huge benefits that "repurposing" of existing drugs (with proven safety profiles) can provide to patients. It was arguably not the EU legislature's intention that valuable research of this nature should be treated in a different manner from research into new active ingredients.

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