Patent term extensions for biosimilars

With an increasing number of biosimilar medicines entering the European market, attention has focused on whether patent holders of the original innovative product can obtain patent term extensions covering such biosimilar medicines to reduce erosion of the research and funding efforts invested in the innovative product.

Patent term extensions in Europe (in the form of a Supplementary Protection Certificate, termed an SPC) exist to compensate patentees for the regulatory delays faced in gaining marketing authorisation approval for patented medicines. Such extensions are for a period of up to 5 years beyond patent expiry and cover authorised medicinal products that fall within the scope of the patent claims.

When we talk about biosimilars, what do we mean?

Biosimilars are medicines of biological origin in which the active substance is comparable to that in an original innovative product. The biosimilar and innovator medicines are used at the same dose to treat the same disease.

Thus biosimilars are different to generic medicines ("copycat" versions of small molecule drugs), because the active substance is not chemically and structurally identical to the original innovative product.

As a result of the heterogeneity, any variation must be assessed to ensure that there is no therapeutic consequence for the patient, and also the biosimilarity needs to be demonstrated through rigorous comparisons of safety, efficacy and quality with the original innovative product. Thus, the regulatory requirements for developing biosimilars are more demanding than for developing generics, where a company has to simply demonstrate bioequivalence with the original innovative product by appropriate bioavailability studies.

In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) is the national body responsible for authorising medicines, including biosimilars. The regulatory framework for authorising biosimilars has been in place in the EU since October 2005. Biosimilars have been on the UK market since 2006 when Omnitrope® (somatropin, recombinant-DNA growth hormone) was launched.

Patent protection for biosimilars

Often patent claims covering the original innovative product are broad enough to cover biosimilar products. The patent claims will also often cover the method of manufacturing the original innovative product and associated products, such as cell lines used to produce the product. These can be broad enough to cover biosimilar products. This allows the patent holder of the original innovative product to recoup some of their research and funding efforts during the patent term without biosimilars entering the European marketplace.

Therefore, during the patent term, it is difficult for another party to develop and launch biosimilar products.

Bolar exemptions exist in Europe, which provide exemptions to patent infringement for certain research activities. However, these are subject to much uncertainty, particularly at a national level. For example, until recently in the UK, the exemption from patent infringement did not apply to activities carried out to obtain approval of biosimilar products. However, on 1 October 2014, the UK provisions changed to allow exemption from patent infringement for all activities necessary for obtaining approval of biosimilar products. Germany has the same approach, but this is not shared throughout Europe.

As a result, once the patent has expired in the UK, biosimilar products could begin to enter the market almost immediately because biosimilar producers can conduct all the necessary studies while the patent is in force, so they are ready to launch when the patent expires. Therefore, patent holders of original innovative products are looking to obtain SPCs in Europe to delay biosimilar product market entry.

What about patent term extensions for biosimilars?

SPCs are granted for a product, which comprises an active ingredient or combination of active ingredients. SPCs only extend the patent protection in respect of authorised medicinal products.

In the case of generics, where the original innovative product and generic product contain the same active ingredient, an SPC for the original innovative product covers the generic product. Therefore, the patent holder of the original innovative product can obtain a patent term extension for up to an additional 5 years beyond patent expiry to keep generic products out of the market in Europe, unless under licence.

However, the same is not always true of biosimilar due to the fact that the active ingredient only needs to be comparable to that of the original innovative

product. Therefore, it is questionable whether an SPC for the original innovative product covers the biosimilar product if the active ingredient in each product is not the same.

Patent holders can currently obtain an SPC for a product based on a marketing authorisation granted to another party. Therefore, the patent holder could seek an additional SPC to the biosimilar product when it obtains its marketing authorisation, provided that the patent protects the biosimilar product and is in force when the biosimilar product is approved.

Determining whether the patent protects the biosimilar product in terms of the SPC Regulation is not a straightforward as it sounds. There is currently uncertainty in Europe as to how to determine whether a patent protects a biosimilar product. The Court of Justice of the EU (CJEU), the highest court in Europe, has ruled that the claims must relate, implicitly but necessarily and specifically to the active ingredient in question. The CJEU explicitly stated that this was not an infringement test, but gave little other guidance. Thus, the actual interpretation of this test has been left to the national courts. For example, for claims to an antibody, it is currently unclear whether claims to a novel protein and antibodies defined functionally by their specific binding to the protein are sufficient to protect specific antibodies, which are not given structurally in the claims. The UK Patents Court has recently ruled that this type of functional definition is acceptable and found an SPC should be granted to the specific antibody that had obtained marketing approval *(Eli Lilly and Company Ltd v Human Genome Sciences, Inc., 2012).* However, this decision is open to appeal and other national courts could interpret the CJEU decision differently. Therefore, in some instances, the patent claims may not be found to protect the biosimilar product, and so the patentee may not be able to obtain an SPC for the biosimilar product.

Also, the question of whether a patent holder that was not involved in obtaining market approval granted to another party can obtain an SPC covering the approved product, is likely to head up to the CJEU at some stage. Some commentators view that because the purpose of the SPC Regulation is to compensate for regulatory delays, only the party who was actually subject to the delays should be eligible for SPC protection. Others view that if the patent would have been infringed by the authorised product, it does not matter who obtained the regulatory approval, the patent holder should be entitled to SPC protection covering that authorised product.

This leaves uncertainty for both patent holders of original innovative products and biosimilars producers as to whether SPC protection can be granted to the patent

holder for biosimilar products protected by their patent claims. This is likely to deter biosimilar developers from applying for marketing approval until patent expiry, since an SPC cannot be obtained on an expired patent. However, if the patent holder has already obtained an SPC for their original innovative product before patent expiry, the patent holder could seek to argue that that SPC also covers the biosimilar product in infringement proceedings. Again, this is currently a grey area, and we are likely in the future to see questions testing the boundary on the scope of SPCs to original innovative products.

Indeed, a recent referral to the CJEU *(E-16/14 - Pharmaq AS v Intervet International BV)* may provide some answers relevant to biosimilars. Intervet have a fish vaccine product (SAV1) that was sold in Norway from 2003 to 2011. Pharmaq have a product which is a molecular variant (SAV3) of the Intervet product (SAV1) and which was held to fall within the scope of the basic Intervet patent in earlier patent infringement proceedings. One of the questions referred to the CJEU asks what the correct process is for determining whether a variant infringes an SPC.

Conclusions

The current state of SPC law leaves much uncertainty for both patent holders and biosimilar producers.

From a patent holder perspective, if the biosimilar product gains marketing approval before patent expiry, the patent holder can currently obtain an SPC for the biosimilar product, provided that their patent claims protect the biosimilar product (see the commentary above). Otherwise, the patent holder can seek to argue in national infringement proceedings that the biosimilar product infringes their SPC for the original innovative product. Hopefully, the recent CJEU referral in the fish vaccines case will provide guidance on this latter perspective.

To assist in both instances, patentees for original innovative products should ensure that their patent claims are drafted broadly enough to cover putative biosimilars, and also exemplify as many putative biosimilars as possible.

From a biosimilar producer perspective, careful due diligence should be performed to check the SPC landscape before making a decision on when to apply for marketing approval.