Patenting Biosimilars

Biosimilars can rapidly receive marketing approval through a streamlined process that allows generic companies to rely upon previous clinical data to enter the market as soon as the innovator company's patent protection expires

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In the world of pharmaceuticals, innovator companies seek to develop products containing novel therapeutic agents such as compounds and biologics. This requires an extensive R&D outlay, both for pharmaceutical products, which will ultimately reach the market, and those that fall at one of the many hurdles along the way. Such companies hope to recoup some of these costs through patent revenue, and obtaining patent protection for an innovative therapeutic agent is thus central to the strategy for developing a product.

For a new therapeutic agent, perhaps the most valuable form of patent protection available is a product claim broadly covering the agent per se as well as related agents considered to possess corresponding therapeutic activity. This will allow the innovator company to prevent a third party from making, using, selling, or importing the company's pharmaceutical product. Depending on the scope of the patent claims, such a patent may also allow the innovator company to prevent a third party undertaking these activities in relation to agents containing only arbitrary modifications. Other valuable forms of patent protection include claims relating to methods of obtaining or manufacturing the agent, formulations of the agent for administration, and combination products including the agent and another pharmaceutical product. In the US, obtaining claims relating to a method of treating a certain condition using the agent is also possible. Such claims are not permitted in Europe as they are considered to unduly restrict medical professionals from treating patients using patented pharmaceuticals. However, claims drafted as medical use claims, ie "compound X for use in a method of treating disease Y", are permitted and provide a similar scope of protection.

Innovative therapeutic agents must be extensively tested before they are given market approval. This can lead to a substantial delay in bringing the product to market. To compensate for this perceived loss of patent term, patentees can apply for a Supplementary Protection Certificate (SPC) in Europe, although similar provisions are not available in the US. An SPC is a national right that extends the duration of a patent insofar as it relates to an approved pharmaceutical product. The extension is granted for a maximum of five years, with an additional six-month extension available if paediatric testing has been conducted. SPCs can be extremely valuable as they are valid at the end of a patent's lifespan when the pharmaceutical product will be at its most lucrative and generics companies will be keen to launch biosimilar products. For this reason, an extension of patent term of only a few days can be worth millions of pounds in revenue to the innovator company.

Biosimilar Products

Over the last decade, the number of available biosimilar products has risen. A biosimilar mimics a therapeutic biologic previously devised and approved for market by an innovator company. Biosimilars can take many forms, including antibodies, proteins, blood products, cells, and gene therapy products. These are often prepared by generics companies as the patent protection surrounding an innovator product approaches expiry and provide a unique opportunity to bring a biologic pharmaceutical product to a market that is already defined and ready and for which an expensive *de novo* clinical trial is not required. Not only is this beneficial to the generics company, it can also reduce the cost of established biologic pharmaceuticals, reducing the monetary burden upon increasingly stretched health services.

Following expiry of a period of data exclusivity, which lasts eight years in Europe and up to 12 years in the US, generics companies can seek regulatory approval for a biosimilar product, although in Europe it may not enter the market until the innovator product has been on the market for a further two years. The approval process for biosimilars is significantly streamlined compared to the more arduous approval process for an innovative pharmaceutical product. For biosimilars, the approval process centres around demonstrating that the biosimilar does not have any meaningful differences compared to the innovator product in terms of quality, safety, or efficacy. The complex nature of biologics means that biosimilars will usually need to be produced using the same method as the original biologic, ensuring sufficient conformity.

The Patenting Process

A biosimilar, almost by definition, should be much too closely related to the original therapeutic biologic for patent protection to be granted for the biosimilar product per se. However, generics companies should check, prior to disclosing their biosimilar product, that no aspect of the product itself could be protected in its own right. Even if product protection is not available, alternative forms of follow-on patent claims may be available and should be considered by generics companies prior to

> **Over the past decade, the blurring of the divisions has evidently increased between traditional innovator companies and traditional generics companies in the pharma sector**

disclosing their biosimilar. Of course, to be entitled to patent protection in its own right, the biosimilar must represent some form of invention, and it is here that generics companies are increasingly turning innovators. Such inventions may relate to a new formulation, method of delivery, or dosage regimen for a known agent. Of course, the potential value of a follow-on patent will be highest if the patented invenion represents a real advantage over what has gone before. However, the ability of a generics company to utilise the abridged biosimilar approval process will be decreased if the new invention represents a substantial departure from the innovator biologic for which marketing approval has already been obtained. The generics company must balance the value of obtaining a patent for its own invention against the vastly increased costs of obtaining marketing approval if the abridged biosimilar approval process is not available.

Perhaps one of the most common forms of follow-on patents claim further medical uses of known pharmaceutical products. These patents arise when a known pharmaceutical product is demonstrated to have the ability to treat a condition for which it was not previously known to be used. Such patents have traditionally related to the treatment of an entirely distinct condition, eg the treatment of obesity with a product previously approved for the treatment of headaches. However, further medical use patents are also increasingly being directed to the treatment of additional patient populations. For example, patents are now being granted with further medical use claims directed to the treatment of patients expressing a particular combination of biomarkers or to the treatment of patients shown not to respond to an alternative therapy. Marketing approval for the treatment of an additional patient population is unlikely to be available using the streamlined biosimilar approval process, and, in this area, generics companies are increasingly being required to conduct full scale clinical trials.

The additional forms of patent protection discussed earlier are available to innovator companies as well as to generics companies developing a biosimilar, as these two types of pharma companies become ever less distinct. Such follow-on patents may provide the innovator company with an extended period of protection for their pharmaceutical product, and generics companies should be sure to identify all relevant patent families prior to launching a biosimilar.

Marketing a Biosimilar

Generics companies often try to clear the way to market a biosimilar using a combination of central opposition proceedings and national litigation to invalidate the innovator company's core patents, including product patents and SPCs protecting the innovative therapeutic compound, as well as any relevant follow-on patents.

Central opposition proceedings at the European Patent Office (EPO) provide a cost-effective way in which generics companies, or other interested third parties, can seek to invalidate a European patent. These proceedings are attractive because they are much cheaper than national litigation and, if successful, can lead to revocation of the relevant patent simultaneously in all European jurisdictions. An opposition can be filed within nine months of grant of any European patent on the grounds that the granted claims are excluded from patentability, lack novelty, lack inventive step (article 100[a] EPC and articles 52-57 EPC), are insufficiently disclosed (article 100[b] EPC and article 83 EPC), or do not have adequate basis in the application as filed (article 100[c] EPC and article 123[2] EPC). Expedited proceedings at the EPO mean that opposition proceedings are now routinely concluded within 15 months. However, decisions of the Opposition Division are open to appeal, and receiving a decision from the Boards of Appeal at the EPO can take up to four years.

National litigation is another route through which generics companies often seek to clear the way to market a biosimilar and is the only route available once the nine month opposition period before the EPO has expired or if an opposition before the EPO is not successful. National litigation proceedings are usually much more costly than central opposition proceedings before the EPO and, of course, will only lead to revocation of the patent in that particular jurisdiction. Starting national litigation proceedings also brings with it the risk that the innovator company will counter-claim for patent infringement in the event that the patent is found to be valid. However, there are also advantages associated with national litigation.

Firstly, it can enable a patent to be revoked on additional grounds, such as the ground of lack of entitlement, which is not considered by the EPO. Secondly, divergent case law in different jurisdictions can lead to a more favourable outcome in one jurisdiction than another, depending upon the facts of the case.

Europe is expecting the imminent introduction of the Unified Patents Court (UPC). This will be a central European court that will eventually deal with most patent disputes in Europe and will represent an additional forum for patent litigation. Together with the European Patent with Unitary Effect (Unitary European Patent), the UPC will seek to combine the positive parts of central opposition proceedings and national litigation. At present, the date of commencement of this long-anticipated system is unclear as Germany's ratification is awaited, which has been delayed due to a complaint filed by an individual to the Germany constitutional court.

Moving Forward

Over the past decade, there has been a blurring of the divisions between traditional innovator companies and traditional generics companies in the pharma sector.

As innovator companies progressively seek to develop biosimilars, and generics companies increasingly seek to develop and patent protect new formulations and new therapeutic uses of existing pharmaceuticals, this division will likely continue to blur, perhaps eventually yielding a single genus of innovator-generic pharma companies.

About the author

Jennifer O'Farrell is a Partner in the biotechnology and life sciences group at Boult Wade Tennant. Jennifer has more than a decade's experience of obtaining, attacking, and defending patents in the biotech field. She has extensive experience prosecuting patent applications before the EPO, as well as attacking and defending patents during opposition proceedings before the EPO, managing clients' international patent portfolios, advising on filing strategies, and prosecuting patent applications before the UK Intellectual Property Office. Jennifer has been extensively involved in the filing of SPC applications throughout Europe.
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