boult

Guide to IP rights and exclusivity for pharma and biotech in Europe

By Dr Nadia Tyler-Rubinstein
and Dr Joanna Peak

Introduction

Patent protection plays a key role in incentivising and rewarding research and development in the Pharma and Biotech sectors. The development of any new drug is a laborious process, often with many years of pre-clinical studies followed by clinical trials in patients prior to the grant of a marketing authorisation (MA). Importantly, innovator companies can spend tens to hundreds of millions taking a drug from the discovery phase through to approval by the regulatory authorities.

The average cost of getting a new drug to market has been estimated to be in excess of £1 billion. Ensuring that innovators have a monopoly when their new drug first hits the market is essential to drive innovation in the healthcare sector. However, to improve patient access to medicines, the manufacturers of generic or biosimilar medicines are allowed to bring their products to the market after a certain amount of time has passed. The presence of generic and biosimilar manufacturers on the market has the potential to introduce competition, lower prices and increase drug supply, potentially benefitting patients longer term.

The timing of generic/biosimilar entry onto the market is governed by a complex interplay of intellectual property (IP) rights and other forms of exclusivity that exist specifically for pharmaceutical and biological products. Although IP rights and other exclusivity rights may overlap, they do not necessarily run concurrently and can cover different aspects of a drug.

These different IP and exclusivity rights are explained in more detail within this report.

The average cost of getting a new drug to market has been estimated to be in excess of £1 billion.

Patents

In Pharma and Biotech, patents typically form the foundation for protecting any new drug product. Patents protecting the active pharmaceutical ingredient (API) are typically most valuable; however, secondary patents can play an important role in extending the innovator's monopoly and thereby restricting generic and biosimilar access to the market.

Composition of matter patents

The first patent to protect the API of a drug product is often termed the "Composition of Matter or CoM" patent.

This terminology stems from US patent law but is a term that has been coined across the Pharma industry. CoM patents typically provide robust patent protection for drug products and the manufacturers of generics and biosimilars regularly look to the expiry date of the CoM patent to assess "loss of exclusivity" for any given drug product.

The maximum term of a European patent is 20 years from the filing date of the patent application. The patent may lapse earlier if the annual renewal fees are not paid or if the patent is revoked. Most innovator medicines are developed under patent protection. This means that third parties cannot make and sell the medicine before the patent term either lapses or expires (unless they have the consent of the patent proprietor).

For regulated substances like pharmaceuticals and biologic drugs, the "effective" patent term conferred by the CoM patent is often much shorter, as much of the 20-year monopoly will already have elapsed before the drug is approved and can be sold. This problem is addressed by the award of additional protection via "Supplementary Protection Certificates or SPCs", as described below.

Supplementary protection certificates

Supplementary protection certificates

A drug that is subject to patent protection and that has also been awarded a marketing authorisation (MA) may be granted an additional term of protection via a supplementary protection certificate (SPC). SPCs are IP rights distinct from patents but the protection they confer is similar to the rights conferred by patents.

SPCs for medicinal products are currently granted in accordance with **EU Regulation (EC) No 469/2009** and are obtained via applications to the national patent offices across Europe. The SPC system exists to compensate patent holders for the effective loss of patent term that occurs due to the compulsory lengthy testing and clinical trials required prior to obtaining marketing authorisation for a medicinal product. SPC protection enters into force when the patent expires and can extend protection for up to an additional five years.

The EU is currently reviewing proposals intended to reform the current SPC system, in particular to improve harmonisation of the system across Europe.

Reform of the EU's SPC system

As noted above, SPCs are applied for and granted by the national patent offices across Europe. Although each patent office applies the criteria set out in EU Regulation (EC) No 469/2009, the granting of SPCs is not particularly harmonised across Europe. There have been many referrals to the Court of Justice of the EU (CJEU) regarding interpretation of the SPC Regulation and yet there is still a distinct lack of clarity regarding the criteria to be applied.

The EU is currently reviewing proposals intended to reform the current SPC system, in particular to improve harmonisation of the system across Europe. These proposals include the introduction of a centralised procedure for the examination and grant of SPCs. This procedure would involve the filing at the EUIPO of a centralised SPC application based on a European patent and a centralised MA granted by the European Medicines Agency (EMA). The EUIPO would act as a central examination authority and issue a single decision to either grant or refuse a bundle of SPCs in all designated Member States in which SPCs are sought. The proposals for reform also include some substantive changes to the law; however, no changes are proposed to the core criteria for obtaining SPC protection and it appears to be the position of the EU Commission that previous CJEU case law is to remain in force.

Unitary SPCs

As part of the reform of the SPC system, a new SPC Regulation is proposed for the grant of Unitary SPCs. Unitary SPCs would complement the Unitary Patent (UP) system which came into force on 1 June 2023. A Unitary SPC would be based on a UP and would be a single right having the same territorial scope as the underlying UP.

Since the territorial scope of a UP is limited to the countries who have ratified the UPC Agreement (currently 18 countries), national SPCs are likely to be needed alongside a Unitary SPC, for example in the UK and Spain.

Trade marks

Trade marks also play a pivotal role in shaping brand identity and consumer trust. Innovators will want to protect their brand via registered trade mark rights since that brand value is what will drive sales in the face of competition, particularly once the product is off patent. There are several unique issues facing those developing new brands in the pharmaceutical sector.

From an inherent registrability perspective, a trade mark must be distinctive enough to enable it to function as an indicator of source origin, that is, to allow consumers to easily identify the products/services being offered under the mark from those of other companies. In addition, there are trade mark availability and infringement considerations, including that the proposed mark is not similar to existing marks on the same or similar medical indications such that confusion is likely to arise.

This is particularly important in the Pharma and Biotech industry where there is a risk that consumers, including healthcare professionals, might confuse one medication for another. This confusion could lead to incorrect usage, dosage errors, or other safety issues, potentially jeopardizing patient health.

Moreover, a mark for a pharmaceutical product must also overcome regulatory hurdles. While national IP offices are responsible for examination and grant of trade marks, it is the regulatory health authorities (e.g. the EMA and MHRA) to which owners must apply to obtain marketing authorisation. Pharmaceutical companies therefore have the difficult task of finding a name that is accepted by both the regulatory authorities and the IP offices.

For instance, a trade mark for a pharmaceutical product must not be too close to or derived from the international non-proprietary name (INN) of the active ingredient, nor should it be confusingly similar to existing trade marks or medicinal products. Moreover, a pharmaceutical trade mark must not make an overt claim as to the effect of the product, nor be misleading as to its effects, safety or composition. There are further complex challenges unique to the pharmaceutical industry, for example, determining a drug's timeline to approval and how that fits in with the vulnerability of a trade mark registration to non-use cancellation.

Regulatory exclusivity

As noted on page 02, exclusivity rights exist for pharmaceuticals and biologics outside the framework of IP rights. More specifically, regulatory bodies, such as the EMA, offer periods of exclusivity for new innovator products. This period of exclusivity is dependent on the drug's approval status.

Data exclusivity

From the date of marketing authorisation, the MA holder benefits from a period of eight years of data exclusivity in which they enjoy the exclusive rights to the results of preclinical tests and clinical trials relating to their drug. Data exclusivity therefore effectively prevents third parties, such as generic or biosimilar companies, from relying on the approved drug's clinical data to support their own regulatory filing. Only upon expiry of the data exclusivity period is the MA holder obliged to release this clinical information to companies wishing to develop generic or biosimilar versions of the medicine.

From the date of marketing authorisation, the MA holder benefits from a period of eight years of data exclusivity in which they enjoy the exclusive rights to the results of preclinical tests and clinical trials relating to their drug.

Market exclusivity

In addition to the period of data exclusivity, the MA holder also benefits from a further two-year period of market exclusivity, during which a generic or biosimilar medicine for the same indication cannot be placed on the market even if it has already received its own marketing authorisation.

Accordingly, regulatory exclusivity provides an important layer of protection for new medicinal products, which is complementary to that provided by other rights, such as patents and SPCs.

Orphan drug exclusivity

An orphan drug is a drug that is developed to treat a rare medical condition. Since only a small population of patients is affected by the condition, development of an orphan drug may not be profitable without additional incentives and compensation. In the EU, orphan medicines benefit from orphan rewards of up to ten years of market exclusivity from similar products for the same indication. This measure is intended to encourage the development of medicines for rare diseases, by protecting them from competition from similar medicines with similar indications, which cannot be marketed during the exclusivity period.

Reform of EU regulatory exclusivity

EU pharmaceutical legislation is currently undergoing reform. The reform packages includes a proposal for a new Directive (replacing 2001/83/EC and 2009/35/EC) and a new Regulation (replacing 726/2004, 141/2000 and 1901/2006), to revise and replace the existing pharmaceutical legislation. While the proposals are ongoing and not yet finalised, we can expect to see changes to the periods for Regulatory Data and Market Exclusivity and Orphan Drug Exclusivity.

Paediatric extensions

The Paediatric Regulation (Regulation (EC) No 1901/2006) has been in force in the European Union since 2007. Its objective is to improve the health of children in Europe by facilitating the development and availability of medicines for children aged 0 to 17 years. Through a series of incentives, obligations and rewards, the Paediatric Regulation ensures that this important area of research is not neglected, such as research into rare childhood diseases.

The Regulation mandates that to obtain a marketing authorisation for a new medicinal product, it is necessary to present the results of studies conducted in the paediatric population in accordance with an agreed paediatric investigation plan (PIP). It is possible to request a PIP deferral if results of the studies are not yet available, or to obtain a waiver if the medicine is not appropriate for use in children e.g. menopause treatments. The PIP will propose measures to adapt the formulation of the medicinal product e.g. by identifying appropriate dosages, so as to make its use more acceptable, easier, safer or more effective for the paediatric population.

These requirements aim to make it an integral part of the development process of any new medicine to at least consider the potential of the medicine to be used in the paediatric population. However, it is not necessary that the results of the studies confirm that the product is safe and effective for use in children. The aim is to encourage paediatric research for its own sake and an authorisation can still be granted even if a paediatric indication is not ultimately authorised.

Upon completion of the agreed PIP studies, the MA holder can benefit from various rewards. For instance, if a paediatric indication is authorised, then the MA holder can apply for and obtain, a one-year extension of the period of marketing protection for the medicinal product concerned, on the grounds that this new paediatric indication brings a significant clinical benefit in comparison with existing therapies.

Alternatively, if the medicinal product in question is designated as an orphan medicinal product pursuant to **Regulation (EC) No 141/2000** and the MA holder has completed the agreed PIP studies, then the ten-year market exclusivity period for orphan drugs will be extended to twelve years. As a further alternative, where PIP studies have been completed, and the medicinal product is protected by an SPC, the SPC holder shall be entitled to a six-month extension of the period. The maximum possible term of an SPC is therefore five and half years.

So when can generic/ Biosimilar companies start their activity/launch?

Although the manufacturers of generic and biosimilar medicines are able to benefit from the work carried out by the original innovator company, the route to market is not simple; years of planning are still required on the part of generic/ biosimilar companies in order to bring their products to market. This is particularly the case for biosimilars where complex manufacturing protocols may need to be devised for the large-scale production of clinical-grade biologics. Generic and biosimilar medicines must also be granted a marketing authorisation, for example by the EMA, in order to enter the market in Europe. Taken together, it can be a lengthy process.

A balance must always be struck between encouraging new drug innovations (i.e. by rewarding innovators) and ensuring patient access to medicines at affordable prices (i.e. by allowing generic and biosimilar medicines to enter the market). Accordingly, various provisions exist that are intended to limit IP rights in certain circumstances. The "Bolar Exemption and SPC Manufacturing Waiver" allow generic/biosimilar companies to start their activities prior to the expiry of any patents or SPCs, respectively.

Bolar exemption

The Bolar exemption traditionally allows manufacturers of generic and biosimilar medicines to benefit from a patent law exemption that stipulates that certain acts required for preparing a corresponding marketing authorisation application are not considered infringing acts. The Bolar exemption aims to encourage earlier generic and biosimilar access after expiry of IP rights and to increase availability of more affordable drugs. As a principle of EU law, the Bolar exemption must be implemented by each Member State into national law. Notably, the different interpretations of the Bolar provisions has resulted in a lack of harmonisation across European countries.

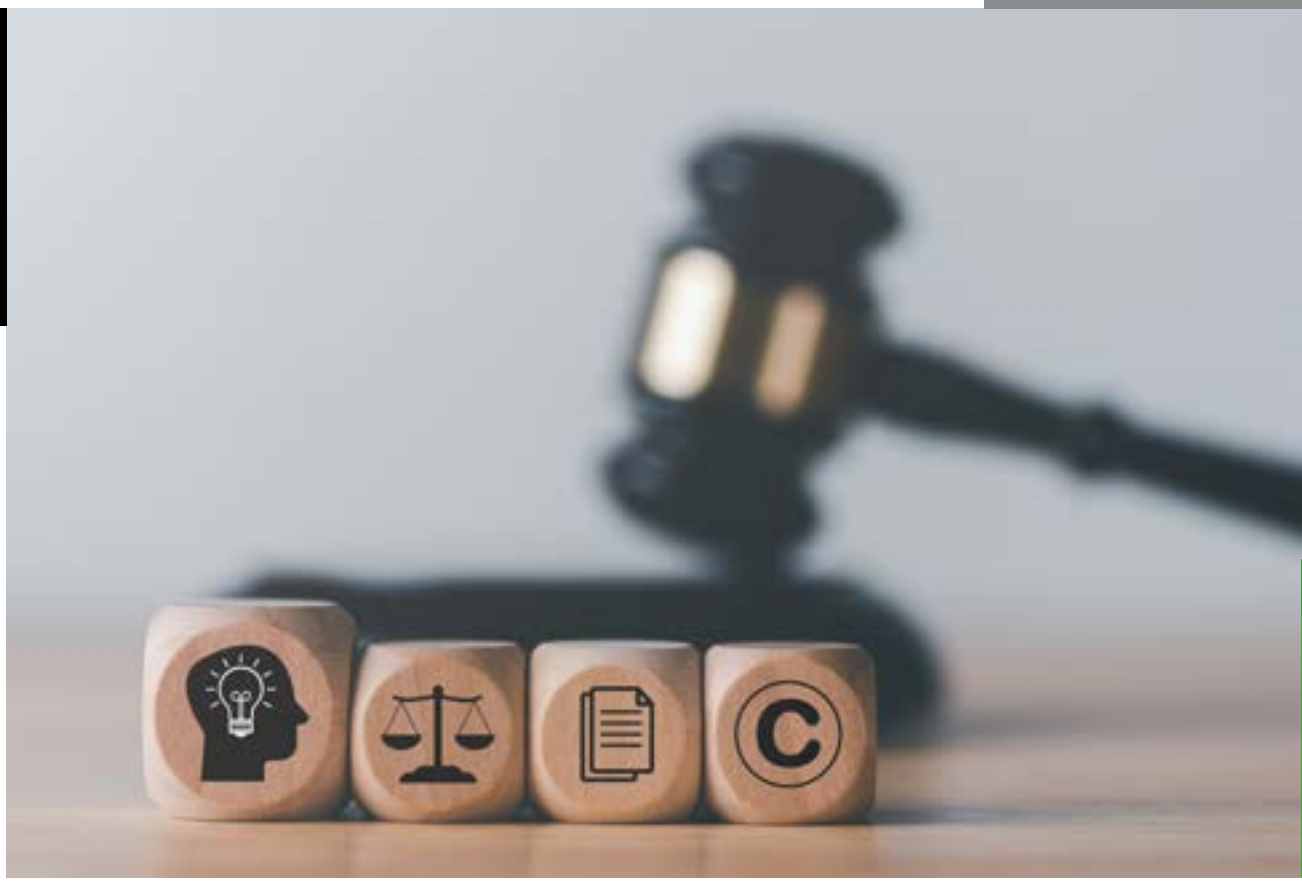
This has led to uncertainty for innovator and generic manufacturers and has resulted in some Member States being more attractive locations than others for generic manufacturers. In practice, the Bolar exemption is intended to permit any studies, tests and trials carried out to show that a generic/biosimilar product is bioequivalent to an approved, patented product, where these acts are required for submitting a marketing authorisation application. The provision also exempts other acts related to pricing and reimbursement activities for generic/biosimilar products. Note that changes to the Bolar exemption are expected as part of the EU pharmaceutical legislation reform package.

SPC manufacturing waiver

The SPC manufacturing waiver introduces an exception to the protection conferred by an SPC. It applies to all SPCs filed on or after 1 July 2019. The waiver permits EU-based generic and biosimilar companies to manufacture an SPC-protected product specifically for export to a non-EU country where patent protection does not exist. In addition, the waiver permits the stockpiling of the SPC-protected product during the final six months before SPC expiry. These measures are intended to ensure that generic and biosimilar manufacturers based in the EU are more effectively able to compete with non-EU-based manufacturers and puts them in a better position to launch in the EU immediately after expiry of the SPC – a practice known as a 'day 1 launch'.

Skinny labelling

Skinny labelling in Europe refers to a practice where a generic or biosimilar drug manufacturer can exclude patented uses or indications from their product label when applying for marketing authorisation, allowing them to sell a generic/biosimilar version of a drug even if certain uses of that drug are still protected by a patent, essentially "carving out" the patented information from the label, thus enabling market entry despite the patent barrier. On paper, skinny labelling appears to be an elegant solution for protecting the rights of both innovators and generics/biosimilars. However, in practice, "cross-label" use occurs often, whereby healthcare practitioners or pharmacists write prescriptions with reference to the INN of a drug, with the result that patients can end up receiving a generic version of a drug to treat a patented indication.



Loss of exclusivity

Once patent protection has expired and regulatory exclusivity periods have also expired, innovator companies face "loss of exclusivity (LoE)" – the time when generic and biosimilar companies are able to enter the market. With the loss of this monopoly, the drop in revenue can be immediate and severe. Although a natural milestone in a drug's lifecycle, innovator companies will look for value-extending strategies to mitigate the effects of LoE.

As noted above, extending patent protection beyond the CoM patent is often a priority with companies looking to rely on the protection afforded by secondary patents e.g. formulation patents, dosing patents etc. The protection afforded by secondary patents is often not an absolute bar to generic/biosimilar entry onto the market and secondary patents are sometimes vulnerable to invalidity attacks. Generic/biosimilar companies looking to enter the market once CoM patents and regulatory exclusivity periods expire may seek to "clear the way" of any secondary patents that present a possible infringement risk – either at the European Patent Office (EPO) or in national litigation.

Once an innovator has exhausted their patent-related strategies, other options remain. These may include:- marketing strategies to preserve brand equity and patient loyalty; switching patients to a next-generation or over-the-counter (OTC) version of the product; surge pricing to maximise earnings prior to patent expiry; as well as special contracts, such as volume discounts, bundled product offerings and service discounts to incentivise channels to stock or dispense preferred brands and inhibit generic substitution. Notably, despite the entrance of generic or biosimilar competitors in the market, for high-affinity brands, patients often exhibit "stickiness" even after LoE.

Glossary

Originator or innovator medicine

An originator or innovator medicine is the drug product that was first authorised based on evidence of its efficacy, safety and quality. The originator company typically incurs the costs of drug discovery and drug development on top of subsequent manufacturing and marketing efforts.

Generic medicine

A generic medicine is developed to be the same as an originator medicine (called the reference medicine) i.e. it contains the same active pharmaceutical ingredient (API), is administered via the same route, at the same dose and for the same intended use. A generic medicine typically refers to a chemically synthesised, small molecule medicine. The manufacturing process is repeatable such that each batch of generic drug contains the same API of the reference product. The generic medicine may differ however in some characteristics such as the formulation, excipients, colour, taste, name and packaging. Since safety and efficacy data is already available from the reference medicine, the generic company may rely on this available data and need only provide evidence of quality and to demonstrate that the generic medicine produces the same level of active substance in the human body. A company can only submit a marketing authorisation application for a generic medicine once the period of data exclusivity of the reference medicine has expired. Moreover, generic medicines can only be marketed once the period of market exclusivity of the reference medicine has expired and upon expiry of any patent rights held by the innovator company.

Biosimilar medicine

A biosimilar medicine is developed to be highly similar to an originator medicine (called the reference biological medicine). Biosimilars are typically larger, more complex biologic molecules produced by living organisms such as bacteria, yeast or animal cells. The inherent variability in living organisms and more complex manufacturing of biological medicines does not allow for exact replication and therefore slight differences will exist between a biosimilar and the reference product it is based upon. Importantly, a biosimilar medicine must be shown not to have any clinically meaningful differences from the originator medicine in terms of safety, quality and efficacy.

Developers of biosimilars are required to demonstrate comparability studies with the reference biological medicine, but can avoid the unnecessary repetition of clinical trials already carried out with the reference medicine. As for generic medicines, a company can only submit a marketing authorisation application for a biosimilar medicine once the period of data exclusivity of the reference product has expired and can only be marketed once the period of market exclusivity and any patent term has expired.

Glossary cont.

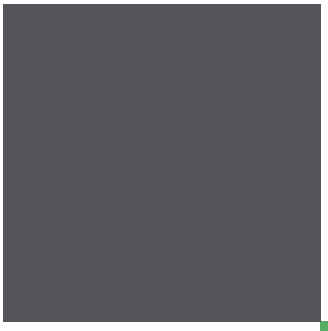
Biobetter

More recently, a new class of biologics have emerged. As the name suggests, "biobetters" are considered to be better, new-and-improved versions of existing originator biologics. Unlike biosimilars, biobetters may have alterations in their molecular structure that results in improved efficacy or safety. Superiority may result from a difference in amino acid sequence or protein folding, from a chemical modification, from polymer conjugation, from a difference in the humanization process etc. Since biobetters are considered as investigational new drugs (IND) they are currently subject to the same non-abridged regulatory procedure as originator drugs.

Marketing authorisation

To market a drug in a European country requires the owner to first apply for and obtain a marketing authorisation from the relevant regulatory authority in that country. For instance, to market a drug in the UK requires the owner to obtain a marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA). Note that a marketing authorisation is required irrespective of whether or not corresponding patent protection exists for the product.

Many drugs are granted marketing authorisation in Europe under the "centralised procedure" which allows the marketing authorisation holder to market the medicine and make it available to patients and healthcare professionals throughout the European Union Member States, Iceland, Norway and Liechtenstein on the basis of a single marketing authorisation. This single marketing authorisation is issued by the European Medicines Agency (EMA) following a scientific assessment of the application.



Boult Wade Tennant LLP
Salisbury Square House
8 Salisbury Square
London
EC4Y 8AP
www.boult.com