How does the EU encourage pharmaceutical innovation?

Ben Brigou and **Jaap Mannaerts** of **NLO** examine the different incentives the EU offers in order to encourage pharmaceutical innovation, including SPCs, regulatory measures and the Bolar exemption

The protection of pharmaceutical products within the European Union is the result of a complex interplay of different mechanisms which all have one thing in common – they are aimed at encouraging pharmaceutical innovation. While not purporting to be exhaustive or covering every detail, this quick-reference guide explains in a basic manner the different mechanisms which are available in the EU. It should be noted that this is a rapidly evolving field, and that the different in-depth studies which were recently published are likely to give rise to further amendments and fine-tuning to the relevant legislation.

Second medical use patents

The member states of the European Union are all contracting states to the European Patent Convention (EPC). Under the EPC, where a substance or composition is already known to have been used in a "first medical use", it may still be patentable for any second or further use, provided that said use is novel and inventive. A new application of a known compound in the form of a defined, real treatment of a pathological condition is thus considered as an invention eligible for patent protection. This principle extends to many further developments of a known compound or therapy, such as new indications, new dosage forms, new treatment regimens, new patient subgroups for known indications, new combination therapies etc.

Legal basis: Article 54(5) EPC (see also e.g. GL/EPO G-VI, 7.1)

"Upon obtaining a marketing authorisation, a period of eight years of data protection is granted. During these eight years, generic manufacturers are prohibited from referring to the data produced by the originator company and enclosed in its application for marketing authorisation."

Supplementary protection certificates

The supplementary protection certificate (SPC) is an intellectual property right applicable to pharmaceutical and plant protection products in the EU. SPCs are granted nationally by the intellectual property office in each member state. An SPC is always linked to a patent and a product which obtained a marketing authorisation. An SPC confers the same rights as the patent on which it is based, but extends only to the authorised product (for any use of the product as a medicinal product that has been authorised before the expiry of the certificate).

SPCs
- protect authorised product after expiry of patent;
- maximum duration of five years;
- export waiver allows manufacturing for export and stockpiling;
- extension of six months possible if paediatric studies are performed.

An SPC enters into force after expiry of the patent and has a duration of up to five years which is calculated as follows: date of first marketing authorisation in the EEA minus date of filing of corresponding patent minus five years.

Although it has been established that SPCs are not available where the basic patent is a new formulation of a known active pharmaceutical ingredient, the exact scope of the SPC regulation is not established and several cases are currently pending at the Court of Justice of the European Union.

A recent change to SPC legislation provides a manufacturing waiver for SPCs (i) applied for on or after July 1 2019, and (ii) all SPCs applied for before July 1 2019 (including granted or which remain pending) and that come into effect on or after July 1 2019, with the waiver only applying to the second category from July 1 2022. The manufacturing waiver allows a product protected by an SPC to be produced within the European Union for export purposes, and allows stockpiling six months before expiry of the certificate.

Legal basis: Regulation (EC) No 469/2009

Regulatory measures

Data protection (referred to as data exclusivity)

Upon obtaining a marketing authorisation, a period of eight years of data protection is granted. During these eight years, generic manufacturers are prohibited from referring to the data produced by the originator company and included in its application for marketing authorisation. After eight years, generics can obtain a marketing authorisation based on the data produced by the originator company. It is noted that (i) data protection extends to pre-clinical tests (Article 10 Directive 2001/83/EC) and (ii) data protection is granted for every new marketing authorisation (i.e. developments which are not part of an existing 'global MA') and thus is applicable to combination products of previously authorized active ingredients.

Data protection
- prohibits generic manufacturers from referring to the data produced by the originator company;
- covers pre-clinical and clinical data;
- duration of eight years.

If a marketing authorisation is granted for a new indication for a well-established substance, a non-cumulative one-year period of data protection is granted. A well-established substance is a substance where at least 10 years have elapsed since the granting of the first marketing authorisation for it. If a classification change in the legal status of a medicinal product has been granted, a period of one year of data protection is granted.

Legal basis: Regulation (EC) No 726/2004, Article 14(11), Directive 2001/83/EC, Article 10

Market protection (referred to as data exclusivity)

Parallel to the eight years of data protection run 10 years of market protection. During these 10 years, a generic medicinal product cannot be placed on the market even though a marketing authorisation has been obtained. Originators with another product for treating the same indication may enter the market. A company willing to undertake studies to create their own full dossier with which to apply for marketing authorisation may do so.

Market protection
- prohibits generic manufacturers from marketing a generic product;
- runs parallel to data protection;
- duration of 10 years;
- extension of one year if approval for new indication bringing significant benefit.

The collective effect of the data protection and market protection period is that eight years after the originator's medicinal product has obtained marketing authorisation, generic companies can submit an application for marketing authorisation using the abridged procedure, whereby they refer to the data produced by the originator company. Should they obtain marketing authorisation, they are, however, not allowed to put the product on the market before the remaining two years of market protection have elapsed.

The market protection period can be extended by one year if a product is approved for one or more new therapeutic indications during the eight years of data protection, and if it brings significant benefits in comparison with existing therapies.

Legal basis: Regulation (EC) No 726/2004, Article 14(11), Directive 2001/83/EC, Article 10

Market exclusivity

If a medicine obtains an orphan designation and maintains it through the authorisation stage, it enjoys 10 years of market exclusivity with the possibility of a two-year extension if research is undertaken according to an agreed pediatric investigation plan (PIP). However, the market exclusivity period can be reduced to six years, if after five years it is established that the medicinal product no longer lives up to the criteria on which an orphan designation was granted.

Market exclusivity
- reward for gaining approval for treatment of an orphan indication;
- duration of 10 years, can be reduced to six;
- extension of two years possible if paediatric studies are performed;
- also blocks marketing of different (but similar) medicinal products for that indication.

The market exclusivity period for orphan medicinal products is different from the market protection period for non-orphan medicinal products as during the market exclusivity period for orphan medicinal products another similar medicinal product used for the same indication cannot obtain marketing authorisation within the EU.

It is possible for a medicinal product to be authorised both for treating an orphan indication and a non-orphan indication. In such cases the product must have two different marketing authorisations with different names and the different regulatory protection mechanisms available for each marketing authorisation run in parallel.

In order to obtain an orphan designation, (i) the disease to be treated must be life-threatening or chronically debilitating; (ii) the prevalence of the disease must be fewer than five in 10,000 persons, or there is no hope of recovering the initial investment without the orphan medicinal product incentives; and (iii) there must currently be no way of treating, diagnosing or preventing the disease, or the new medicinal product must be of significant benefit compared to existing methods. The request for orphan designation can be filed anytime during the medicinal product development process before the application for marketing authorisation is made, while the application for marketing authorisation typically demands more clinical data. This means that multiple medicinal products can receive an orphan designation for the same indication, while only the first to obtain marketing authorisation can enjoy the 10 years of market exclusivity.

A single medicinal product may obtain multiple orphan designations and can obtain marketing authorisation for one or more orphan as well as non-orphan indications.

Legal basis: Regulation (EC) No 141/2000, Article 8(1), Regulation (EC) No 1901/2006, Article 37

Paediatric incentives

Extension of duration of certificate

Should studies agreed upon with the authorities in a Paediatric Investigation Plan (PIP) be undertaken, a six month extension of the SPC can be granted. This also applies where completion of the agreed PIP fails to lead to the authorisation of a paediatric indication, but the results of the studies conducted are

reflected in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned. However, the extension of the certificate shall only be granted if the product is authorised in every EU member state.

The extension of the certificate is not available for orphan medicinal products or if a one year extension of market protection is obtained.

Legal basis: Regulation (EC) No 1901/2006, Article 36

Extension of market exclusivity

If the product for which a PIP is undertaken is an orphan medicinal product, a two year extension of the regulatory market exclusivity period enters into force instead of the six month extension of the SPC, even if an SPC has been granted.

Legal basis: Regulation (EC) No 1901/2006, Article 37

"The Bolar exemption allows companies to research generic products before the original patent (and potential SPC) has expired, without infringing the patent."

Specific mechanism

The specific mechanism is an exception to the free movement of goods through the European Union which allows a patent or supplementary protection certificate holder to block parallel import of pharmaceutical products from EU member states where such protection could not be obtained before their accession to the EU.

Legal basis: Annex IV (2) of the Act of Accession, signed on April 16 2003

Bolar exemption

The Bolar exemption allows companies to research generic products before the original patent (and potential SPC) has expired, without infringing the patent. The Bolar exemption, however, only allows production of a patent-protected active ingredient for experimental use. This means that stockpiling, i.e. mass producing the medicinal product during the protection period, for immediate sale after end of said period is not allowed under the Bolar exemption. The theoretical effect of this is that generic producers can develop their generic version of a medicinal product even though it is patent-protected, but they cannot commence large-scale manufacturing in the EU until after the expiry of the patent or SPC (see however, our earlier comments on the manufacturing waiver for SPCs). In practice, the Bolar exemption was implemented into the national law of the EU member states in different ways in some member states the Bolar exemption only covers research for generic MA's, while in other member it is also covers research with innovative products.

Legal basis: Directive 2001/83/EC, Article 10(6) and Directive 2001/82/EC, Article 13(6).

Research exemption

A research exemption is provided for in the national laws of all EU member states. For those countries, which have implemented a 'narrow' version of the Bolar exemption, the research exemption continues to be relevant, e.g. when clinical trials are conducted in relation to innovative medicinal products. The scope of the research exemption varies by jurisdiction. Some EU member states have developed a significant body of case law relating to the scope of the research exemption, while in some member states this is largely uncharted territory.

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