REDDIE & GROSE

Pharmaceutical and Life Sciences Group Newsletter - Spring 2020

Welcome to our Spring 2020 Pharmaceutical and Life Sciences Newsletter. In this edition, we provide a comprehensive discussion of developments with SPCs and general intellectual property protection in the Pharmaceutical and Biotech space.

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We hope that you will find this newsletter interesting. However, do please let us know if you would no longer like to receive our client newsletters.

A Whistlestop Guide to SPCs:

Andrew Carridge, Senior Associate, Cambridge

Supplementary Protection Certificates (SPCs) are European *sui generis* rights which provide a form of patent term extension available in Europe for medicinal products or plant protection products.

The period of effective patent protection for medicinal products and plant protection products can be significantly less than in other sectors because of the need to obtain a marketing authorisation (MA).

Obtaining an MA can take a significant amount of time (typically around 12 years), which can be a large portion of the lifetime of a patent (20 years from its filing date).

SPCs are national rights available in individual EU countries (and European Economic Area (EEA) countries: Switzerland and Norway) which are governed by EU regulations. They will also continue to be available in the UK following its exit from the EU.

The SPC sphere is a fascinating and extremely active area of intellectual property law. There is a steady stream of decisions from the Court of Justice of the European Union (CJEU) attempting to clarify the SPC Regulations, and there are a number of issues outstanding. This brief guide attempts to give a sense of the current state of play.

What is the duration of an SPC?

- The term of an SPC is equal to the period of time between the filing date of the basic patent and the date of the first relevant marketing authorisation in the EEA, minus five years, but the maximum duration is 5 years.

- A Paediatric Extension can extend the duration of an SPC by 6 months.

What protection does an SPC provide?

- An SPC confers substantially the same rights as the basic patent and is subject to the same limitations and obligations, but the scope of protection of an SPC extends only to the product authorised to be placed on the market, rather than extending the protection of the whole claim scope of the basic patent.

- For SPCs applied for after 1 July 2019, European generics and biosimilar manufacturers can manufacture products which are protected by an SPC, for export to markets outside the EEA where protection does not exist or has expired. In addition, European generics and biosimilar manufacturers can manufacture and stockpile medicines that are protected by an SPC in the

Member States during the six months before expiry of the SPC, thus allowing them to launch the product in the EEA on the day after expiry of the SPC.

Who can apply for an SPC?

- An applicant for an SPC must own the basic patent. However, the applicant does not have to hold the relevant MA. So, an SPC can be obtained on the basis of a third party MA (C-181/95 (*Biogen v SKB*)).

- It has become common practice that SPCs are granted to owners of the basic patent who rely on an MA held by a third party, including even a competitor, without the consent of that third party. Unlike similar types of patent extensions in Japan and the US, there is no legal provision expressly calling for any specific relationship or agreement between the SPC applicant, and the holder of the MA.

When should you apply for an SPC?

Within 6 months of either:

a) the date on which the marketing authorisation to place the product on the market was granted in the member state in which the application was filed; or

b) the date on which the basic patent was filed.

Where can you get an SPC?

- In an EU country (and/or European Economic Area (EEA) country: Switzerland, Norway) in which a basic patent is in force covering the product and where there is a marketing authorisation in place to put that product on the market in that country.

- The basic patent can either be a national patent or a European patent which has been validated in a contracting state.

- The marketing authorisation can be a national marketing authorisation issued by that particular country, or a centralised (Community) marketing authorisation issued by the European Medicines Agency (EMA).

- There is no centralised SPC. One must apply for an SPC in each individual country in which one is desired.

What is eligible for protection in an SPC?

- Medicinal products defined as “any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to

human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals".

- "Product" is defined as the "active ingredient" or combination of active ingredients. A substance that does not have any therapeutic effect of its own and is used to obtain a certain pharmaceutical form of a medicinal product is not covered by the concept of 'active ingredient' (C-210/13 (*GSK*)).

- Plant Protection Products – defined as "active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to:

  (a) protect plants or plant products against all harmful organisms or prevent the action of such organisms, in so far as such substances or preparations are not otherwise defined below;

  (b) influence the life processes of plants, other than as a nutrient (e.g. plant growth regulators);

  (c) preserve plant products, in so far as such substances or products are not subject to special Council or Commission provisions on preservatives;

  (d) destroy undesirable plants; or

  (e) destroy parts of plants, check or prevent undesirable growth of plants".

- "Active substance" is defined as substances or microorganisms including viruses, having general or specific action against harmful organisms; or on plants, parts of plants or plant products. Active substance" may cover a substance intended to be used as a safener, where that substance has a "toxic, phytotoxic or plant protection action of its own".

What are the conditions for getting an SPC?

One may obtain an SPC if, in the member state in which the application is submitted and at the date of application:

(a) the product is protected by a basic patent in force;

(b) a valid authorisation to place the product on the market as a medicinal or plant product has been granted

(c) the product has not already been the subject of a certificate; and

(d) the authorisation of b) is the first authorisation to place the product on the market as a medicinal/plant product

a) When is a product protected by a basic patent in force?

- A "basic patent" is a patent which protects a product as such; a process to obtain a product; or an application of that product. This can either be a national patent, or a European patent designating the member state in which the SPC is lodged.

- A product composed of several active ingredients is "protected by a basic patent in force" where "even if the combination of active ingredients of which that product is composed is not expressly mentioned in the claims of the basic patent, those claims relate necessarily and specifically to that combination. For that purpose, from the point of view of a person skilled in the art and on the basis of the prior art at the filing date or priority date of the basic patent:

  (i) the combination of those active ingredients must necessarily, in the light of the description and drawings of that patent, fall under the invention covered by that patent, and

  (ii) each of those active ingredients must be specifically identifiable, in the light of all the information disclosed by that patent." (C-121/17 (*Teva v Gilead*))

- What if a single active ingredient is defined in the patent by reference to a Markush structure? Awaiting clarification from CJEU (C-114/18 (*Sandoz v Searle*)).

- What if a single active ingredient is defined in the patent by a functional claim? In the context of an antibody at least, it is not necessary for an active ingredient to be identified in the claims of the basic patent by a structural formula. However, where the active ingredient is covered by a functional formula in the claims, it must be possible to conclude that on the basis of those claims, interpreted *inter alia* in the light of the description of the invention as required by Art. 69 EPC and the protocol on its interpretation that the claims relate implicitly, but not necessarily and specifically, to the active ingredient in question (C-493/12 (*Eli Lilly v Human Genome Sciences*)).

- We are awaiting further guidance from the CJEU on the functional definition of active ingredients and eligibility for SPC protection (C-650/17 (*Royalty Pharma*)).

b) What is a valid authorisation?

- The authorisation must be for a product that includes the relevant active ingredient. So, if the MA is for a product that includes A, it can serve as the basis for an SPC for A, even if the MA is for a combination of A + B (C-322/10 (*Medeva*); C-422/10 (*Georgetown University*))

- SPCs cannot be obtained on the basis of an "end of procedure notice", i.e. on the basis of a notice of an agreement to to grant a MA under the decentralized procedure (the procedure for authorising medicines in more than one EU Member State in parallel), but the relevant authority has not yet taken the step to actually grant it. (C-567/16 (Merck))

- SPCs cannot be obtained on the basis of an authorisation of a drug-device combination product obtained under the Medical Devices Directive (Directive 93/42/EC), i.e. "a CE certificate" (C-527/17 (*Boston Scientific Ltd*))

c) When has a product not already been the subject of an SPC?

- The holder of more than one patent for the same product cannot be granted more than one SPC for that product.

- If a product is protected by a number of basic patents which belong to different patent holders, SPCs can be granted to each of those patentees. This may include the situation where: 1) patent holder A has a patent which protects the product *per se*; 2) patent holder B has a patent for a process for making the product; and patent holder C) has a patent for a therapeutic use of that product.

- Multiple SPCs can be granted on the basis of the same patent, provided that each of the products in respect of which an SPC is sought, is protected as such by the basic patent.

  If a patent owner already has an SPC for a combination of active ingredients, they may be entitled to a further SPC for one of those active ingredients alone which, individually, is also protected as such by the patent (C-484/12 (*Georgetown*)).

  If an SPC has already been granted for a single active ingredient, and a later application is filed for an SPC for a combination containing that active ingredient, the later SPC could be granted in these circumstances particularly if the combination provides a solution of technical problem beyond the monotherapy alone ((C-443/12 (*Actavis v Sanofi*); C-577/13 (*Actavis v Boehringer*))

- If an applicant has previously been granted an SPC for a product which is protected by a basic patent in force for the product *per se*, are they precluded from being granted an SPC concerning a new use of the product in the case where the new use constitutes a new therapeutic indication which is specifically protected by a new basic patent? Awaiting clarification from CJEU (C-354/19 (*Novartis*)).

d) What constitutes the first authorisation to place the product on the market?

- An earlier marketing authorisation does not preclude the grant of an SPC for a different application of the same product provided that the application is within the limits of protection conferred by the basic patent (C-130/11 (*Neurim*)). So, an earlier authorisation which is outside the scope of a basic patent should not be taken into account. In this specific case, the earlier authorisation was for a veterinary use (use in regulating the seasonal breeding activity of sheep) which was outside the scope of the basic patent, the basic patent covering human use in treating insomnia.

- There has been a lack of clarity as to how broadly *Neurim* should be interpreted, but there has been some recent guidance [see below]:

  SPCs cannot be granted for new formulations of previously approved active ingredients, even if the MA for the new formulation is the first one that falls within the scope of the basic patent relied upon for the SPC filing (C-433/17 (*Abraxis*))

  Further guidance is expected shortly from the CJEU C-673/18 (*Santen*) – see Robin Ellis's article below.

What happens to SPCs in the UK now the UK has left the EU?

- The Patents (Amendment) (EU Exit) Regulations 2019 come into effect at the end of the transition period on 31 December 2020. These regulations will bring current EU legislation into UK law as far as possible, to maintain current systems and processes.

- Authorisations from the EMA will be converted into equivalent UK authorisations on 1 January 2021.

- An SPC that has already taken effect in the UK will remain in effect after 31 December 2020. SPCs granted but not yet in force will come into force at the end of the associated patent term, as normal. A pending SPC will continue to progress. There is no need to refile.

- Current EU law provides for a 6-month extension to SPCs which protect medicines that have been tested for paediatric use. From 1 January 2021, the availability of this extension will be determined based on equivalent provisions in the UK's Human Medicines Regulations 2012.

- The SPC Manufacturing Waiver came into force after the Patents (Amendment) (EU Exit) Regulations 2019 were made on 4 April 2019, so it has not yet been fixed into UK law, but the intention is that UK law will be changed to bring the manufacturing waiver into effect.

Interpreting Article 3(a) of supplementary protection certificates (SPCs) regulation with respect to combination products

Robin Ellis, Partner, Munich

At the end of 2019, a decision from the Court of Appeal of England & Wales (EWCoA) in *Teva vs Gilead* gave us an idea of how national courts will interpret the CJEU's latest guidance on the meaning of Article 3(a) – what is a "*product … protected by a basic patent in force*"?

It is an interesting aspect of European law that a decision of Europe's highest court, the Court of Justice of the European Union (CJEU), still has to be interpreted by the national courts when deciding a case in their jurisdiction. This means that if there is anything ambiguous in the decision of the CJEU, national courts throughout the European Union may still come to different decisions!

The background

The *Teva vs Gilead* case was one of three referrals to the CJEU relating to the question of "what is the meaning of Article 3(a)?". In addition to the *Teva vs Gilead* referral – also referred to as the *Truvada* case (C-121/17) – there are the *Prezista* (C-114/18) and *Januvia* (C-650/17) cases.

All of these referrals have one thing in common: the "product" (or at least a part thereof) was not known as an active pharmaceutical ingredient at the effective filing date of the patent.

Truvada is a combination of tenofovir disoproxil and emtricitabine for the treatment of HIV. Although tenofovir disoproxil was disclosed in the patent, emtricitabine was not and it was also not known to be effective in the treatment of HIV until many years after the fling date of the patent.

Prezista is another HIV treatment relating to the drug darunavir but instead of disclosing the structure or chemical formula of darunavir the patent only contains a Markush formula that could, according to experts at trial, cover between 7×10^{135} and 1×10^{377} compounds.

And finally *Januvia*, which relates to the compound sitagliptin for the treatment of diabetes mellitus type 2, is based on patent claims defining a class of compounds as activity-lowering effectors of dipeptidylpeptidase IV (DP IV)-enzymatic activity. Nowhere in the patent is the structure or chemical formula of sitagliptin disclosed.

These facts are important because they give perspective as to why the meaning of Article 3(a) is being questioned. The problems have arisen because the patents (not just the claims) did not structurally identify the "product" in question.

What the courts say

In Truvada, the CJEU provided a "two part" test to determine whether a "*product is protected by a basic patent in force"*. This test essentially requires that:

- the product must *necessarily* fall under the invention covered by the patent; and
- a person skilled in the art would have been able, in the light of all the information contained in a patent, on the basis of the prior art at the filing date or priority date of the patent in question, to *derive the product in question*.*

** This "two part" test has been supported by the preliminary opinion of the Advocate General (AG) in Prezista and Januvia handed down in September 2019 but we are still waiting for the CJEU's judgement.*

Unfortunately, the EWCoA decision only dealt with "part one" of the test. The judgement concluded that the combination product *Truvada* does not *necessarily* fall under the invention because the only claim in the patent relates to a pharmaceutical composition comprising tenofovir disoproxil and optionally other therapeutic ingredients.

So, an optional, unspecified, active ingredient does not "*necessarily"* fall under the invention.

What is not clear is whether the outcome would have been the same if the claim related to a pharmaceutical composition comprising tenofovir disoproxil and optionally emtricitabine?

The conclusions we can draw from the CJEU & EWCoA decisions are that failing to specifically identify combinations of active ingredients in a patent is likely to lead to problems if you want to rely of this patent for an SPC on a combination product. It may even be that in the future, data supporting the effect of this combination will be necessary.

"Part two" of the test was not directly addressed in the EWCoA's judgement, but it was commented on at the end of the decision and one thing is clear, if the product did not even exist at the effective filing date of the patent, it is unlikely to be considered protected by the patent.

What does the future hold?

So where does this all leave us? There is a lot of debate about the impact this decision, and the opinion of the AG in *Prezista* and *Januvia*, could have on future patent drafting in both the small molecule and biotech sector. I do not think much – if

anything – needs to change but below are a few points that are certainly worth bearing in mind:

- the scope of protection of a patent – i.e. the broadest claim – does not have to be limited to the specific product that is the subject of the SPC but;

- don't expect a patent to meet the requirement of Article 3(a) if the product to be protected did not even exist at the effective filing date of the patent;

- if the product did exist at the effective filing date, at least disclose it in the description of the patent and at best include evidence that it treats the disorders for which the product is authorised; and

- if the invention is meant to cover a combination then explicitly disclose (and ideally claim) that combination, don't make the presence of additional active ingredients optional.

Proof that the product actually existed and was intended to fall within the scope of the claims will go a long way to meeting the requirements of Article 3(a). For example, providing the chemical formula/INN of a small molecule; referencing a deposited biologic; or disclosing a specific combination of active ingredients, will all help to support the argument that a *product is protected by the basic patent in force*.

As a final point, it is worth noting that this may not be good news for companies working only in drug discovery, where the final target product is not always known, but it looks as though the trend in Europe is going back towards SPCs compensating for obtaining drug approval and not drug discovery.

The slow death of Neurim - Will SPCs for new indications soon be a thing of the past?

Robin Ellis, Partner, Munich

In January 2020, the Advocate General (AG) provided his opinion in *Santen v INPI* relating to how Article 3(d) of the SPC regulation should be interpreted. An AG opinion is not a final judgement but it is a suggestion to the judges of the Court of Justice of the European Union (CJEU) on how they should decide a case.

This opinion from the AG is interesting and important for two reasons:

1. It is trying to clear up almost 10 years of confusion that was caused by the *Neurim* judgement; and

2. The recommendation provided is very clear.

If the CJEU choose to follow the AG's guidance then *Neurim* could be assigned to the history books and Article 3(d) will, once again, mean what is says.

The background

As a quick reminder, Article 3(d) of the SPC regulation states that a certificate shall be issued if: *"the authorization [for the product] is the first authorization to place the product on the market as a medicinal product".*

The "medicinal product" and "product" are defined in Article 1 of the regulation and essentially relate to "*any substance or composition presented as having curative or preventive properties with regard to human or animal diseases"* and *"the active ingredient or the composition of active ingredients in a drug"* respectively.

It is important to note that this language is more in line with the approach in the US of "one PTE per NCE" and very different from the accepted practice in Japan of getting multiple SPCs on multiple patents relating to the same product/NCE.

Indeed, this narrow, literal, interpretation of the Regulation was the accepted practice in Europe until the *Neurim* judgement in 2012. Without going into the detail of the *Neurim* decision it essentially redefined the definition of "product" in Article 3(d) to be:

"a previously authorised product reformulated into a later authorised medicinal product wherein the basic patent does not protect the previously authorised product"

This positioned Europe somewhere between Japan and the US in allowing more than one SPC on a previously approved active ingredient but for the last 10 years, the question has been how close to the Japanese approach should the *Neurim* judgement take Europe.

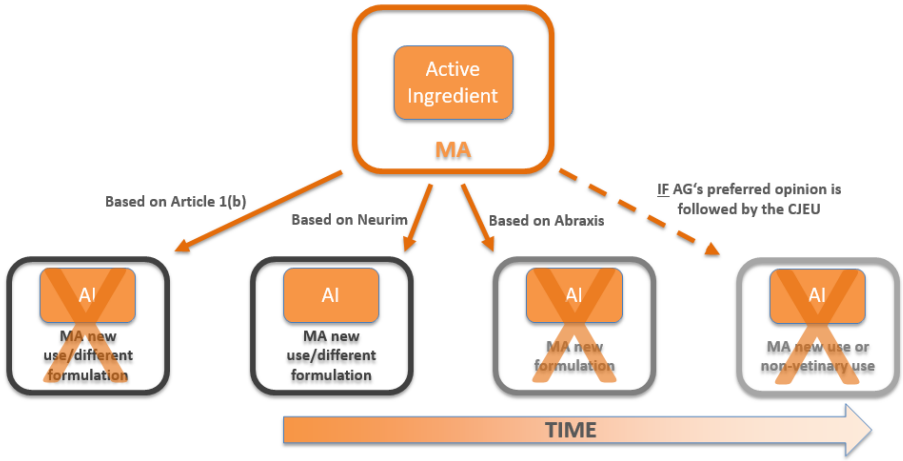

Fig. 1: how the scope of Neurim has been limited over the years and that we may soon be back to an interpretation closer to the literal wording of the Regulation.

In the recent *Abraxis* judgement, the CJEU decided that the *Neurim* interpretation should not relate to new formulations of previously authorised products.

This has now been followed by the Advocate General's opinion in which he goes to great lengths to explain why *Neurim* is inconsistent with both the *Abraxis* decision and existing CJEU case law relating to Article 1.

Following this in-depth analysis, the Advocate General gives the CJEU two options:

- either acknowledge that the teleological approach adopted by the Court in *Neurim* was wrong and should be abandoned; or

- accept the *Neurim* judgement applies only in cases where the marketing authorization, which serves as basis to the request for a SPC, covers a new therapeutic indication of a previously authorised active ingredient or relates to a use in which the active ingredient exerts a new pharmacological, immunological or metabolic action of its own.

There is no doubt which option the Advocate General prefers. In paragraph 17, he concludes that the interpretation adopted by the Court in *Neurim* should be abandoned and dedicates the next 46 paragraphs to explaining how he reached this conclusion. In contrast, he dedicates just 10 paragraphs to reluctantly justify the alternative interpretation.

So, if the CJEU do follow the recommendation of the Advocate General, what would that mean for the pharmaceutical industry?

It is fair to say that nobody has been confident in the strength of SPCs based on new indications of old products but following *Neurim* these were still getting granted, and

a granted SPC, with the backing of a CJEU judgement, can be very valuable in preliminary infringement proceedings. Irrespective of their strength they were keeping generics off the market and/or forcing indications to be carved-out.

If the CJEU chooses to abandon *Neurim* there will be clear guidance that these SPCs should not be granted or are not valid and this could significantly hinder the enforcement strategies of pharma and biotech companies for the next few years. That said, for companies only viewing these SPCs as "upside" when assessing exclusivity for their product, the impact will probably be manageable.

But what about companies whose business model is built around "re-purposing" old medicines?

Developers of personalised medicines; orphan drug developers and companies using big data and AI to identify new, unmet, therapeutic uses are all likely to rely more heavily on this type of SPC to give them valuable additional years of exclusivity. For them, a decision to abandon *Neurim* could have serious commercial consequences.

At the end of the day, although the Advocate General's recommendation would undoubtedly bring clarity to Article 3(d) there will still be many who would prefer things to stay as they are.

Patents are only part of the pharma picture

Andrew Carridge, Cambridge

When it comes to “exclusivity” in the pharmaceutical and biopharmaceutical fields, patents and supplementary protection certificates (SPCs) are not the only options. In Europe, it is important to consider another layer of exclusivity, associated with regulatory data.

Data exclusivity

Before a medicinal product can be put on the market in Europe, it must receive a marketing authorisation (MA). For new active substances, a full application must be made. As part of a full application, the applicant must provide certain information including sufficient preclinical and clinical trial data to demonstrate that the product is safe and effective.

For active substances that are not new, a MA may be granted based on an ‘abridged application’, which can refer to the information provided as part of the application for a first ‘full application’. This allows a company to demonstrate the efficacy and safety of a product whilst avoiding excessive and repetitive testing on human subjects. This is the route commonly sought by generic companies.

A company that has secured a MA on a product for the first time benefits from a period of ‘data exclusivity’ in which the market authorisation holder’s pre-clinical and clinical trial data cannot be used in an abridged application by a third party. However, it does not prevent another company submitting a full-application based on their own clinical trials.

The 8+2+1 regime

Data exclusivity lasts for **eight years** from grant of the MA. After eight years, a third party can use the clinical trial data of the original MA in their applications, but they are not able to market their product until after **ten years** from the grant of the MA.

In some circumstances, the ten year period can be extended by **one year** to a maximum of eleven years. This may be possible if, during the first eight years, the market authorisation holder obtains an authorisation for one or more new therapeutic indications which are held to bring a significant clinical benefit in comparison with existing therapies. A significant clinical benefit could be improved efficacy, improved safety, or a major contribution to patient care (such as a new mode of administration which can be easily self-administered). One example of where a new indication could bring significant clinical benefit is where there is no existing treatment at all for that particular disease.

'Stand-alone' shorter periods of data exclusivity

Where an application is made for a new indication for a well-established substance, a non-cumulative period of **one year** of data exclusivity can be granted, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication.

Medicinal products are classified according to whether or not they are subject to a medical prescription. Where a change of classification of a medicinal product has been authorised on the basis of significant pre-clinical tests or clinical trials, the regulatory authority shall not refer to the results of those tests or trials when examining another application by another applicant for or holder of a MA for a change of classification of the same substance for **one year** after the initial change was authorised. So, if classification data is changed, there is a data exclusivity period of one year.

Orphan drugs

In Europe, a market authorisation holder may obtain **ten years** of market exclusivity following grant of a MA for an orphan drug. An orphan drug is one which is intended for the diagnosis, prevention or treatment of:

a) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people) when the application is made; or

b) a life-threatening, seriously debilitating or serious and chronic condition that, without incentives it is unlikely that marketing the medicine would generate sufficient return to justify the necessary investment.

No satisfactory method of diagnosis, prevention or treatment of the condition concerned must already be available, or, if such a method exists, the drug must be of significant benefit to those affected by the condition.

An additional **two years** of market exclusivity may be available for paediatric medicines, if certain paediatric studies are undertaken.

An application for orphan drug status is separate to a MA application, so orphan drug exclusivity is independent of data exclusivity. Consequently, a drug designated as an orphan drug may benefit from a market exclusivity which runs in parallel with the basic market exclusivity if the drug is also authorised (through a separate MA) for other indications. Any additional orphan indication for the same product benefits from its own period of marketing exclusivity.

What are the implications of Brexit?

In Europe, exclusivity associated with regulatory data is governed by European Union Directives and Regulations. So what will happen in the UK post-brexit?

It is expected that transitional legislation will ensure that ‘centrally authorised products’ (i.e. those products which have been through the European Medicines Agency (EMA) approval process resulting in a single approval for the whole of the EU) will benefit from an automatic UK MA.

A Directive concerning the 8+2+1 regime has already been implemented in UK law by the Medicines Act, and so UK law will largely replicate EU law, at least initially. The UK also has its own regulatory body which handles MAs in the UK (the Medicines and Healthcare products Regulatory Agency (MHRA)), which deals with applications for authorisations of medicinal products. However, in terms of administration, it is not clear whether MAs issued by the MHRA will automatically become valid in the UK, or if separate applications would be required in the EU and UK. One proposal has been implementation of a new assessment procedure based on a review of a positive opinion from the EMA. If MAs issued by the EMA do not automatically become valid in the UK, it is likely to place a significant extra administrative burden on the MHRA and market authorisation seekers.

Current EU law means that the MHRA does not have authority to grant MAs for all medicinal products for all medicines. Presently, certain types of medicines must be assessed in a central procedure by the EMA, such as cancer treatments and orphan drugs. So, if the MHRA is expected to begin examining applications for products that currently fall under the EMA’s authority, it may further add to their burden.

The EMA is based in London, but it appears likely that it will move to an EU state post-Brexit. It is anticipated that such a move is likely have a knock-on effect for users, such as delays in assessing applications.

Artificial intelligence and antibiotics: overcoming excluded subject-matter hurdles

Chris Smith, Senior Associate, London

Drug discovery is expensive. Computers are an important tool in combating this, because their computations can reduce the number of time-consuming physical tests needed. The use of computers in drug discovery is the subject of a great deal of research and we saw an example of this in the news last week when it was reported that a powerful new antibiotic had been discovered using artificial intelligence (see J. Stokes et al., "A Deep Learning Approach to Antibiotic Discovery", Cell, vol. 180, no. 4, pp. 688-702.e13, 2020. Available: 10.1016/j.cell.2020.01.021, widely reported by the media).

Given the investment made in computer processes to assist in drug discovery, we can expect owners of any inventions to want to protect their investment using the patent system. But, patent applications in this field face particular difficulties due to the restrictions on patenting inventions that relate to excluded subject-matter, such as computer programs and mathematical methods. This is a problem when a new drug discovery process relies on advances made in computer programs and mathematical methods.

The news of this antibiotic presents a timely case study to look at how the pharmaceutical industry might protect its investment in any new computer-assisted drug discovery process.

Excluded subject-matter at the EPO

The European Patent Office (EPO) will not grant a patent to an invention that relates solely to any of a number of categories of excluded subject-matter, including computer programs and mathematical methods.

Even if the invention as a whole is more than 'just' a computer program, any steps or features that relate solely to one of these categories of excluded subject-matter will be ignored when assessing inventive step, unless they form part of a 'technical' solution to a 'technical' problem.

Where the invention lies in the use of a computer program or a mathematical method we need to look closely at how it interacts with the claimed system or method as a whole. This includes what effect this feature has on its output.

Could the AI-assisted drug discovery process be patentable at the EPO?

The article above reports that the process of obtaining the antibiotic included the following steps:

- The researchers trained a neural network to predict molecules with antibacterial activity through optimisation over a training set, including 2,000

compounds and results of each compound's effectiveness in inhibiting bacterial growth.

- Once trained, the researchers applied the neural network to a library of around 6,000 compounds under various stages of investigation for human diseases, identifying compounds predicted to have antibacterial activity.

- The researchers then identified candidate compounds for further study by prioritizing compounds among those predicted to have antibacterial activity that are structurally dissimilar to existing antibiotics.

Regardless of the EPO's excluded subject-matter restrictions, it is unlikely that a patent could be obtained for the basic idea of using a neural network to assist the antibiotic discovery process because it is known to use a neural network to assist in drug discovery (see this article in Nature for example). So the mere use of the neural network will not confer inventive step.

The step of prioritizing compounds that are structurally dissimilar to existing antibiotics looks more promising. This step appears to solve a problem that arises in the context of antibiotics and so might not be obvious from any general teaching of neural networks in drug discovery. But the prioritizing step is a step of ordering a list of candidates on a computer and might not be 'technical' by itself. We must be able to demonstrate that this step forms part of a technical solution to a technical problem. If not, the EPO could simply ignore it when assessing inventive step. One way to demonstrate this is if the step has some physical effect in the real world, as opposed to producing results that are confined to data in a computer. This is because the real world is generally viewed as 'technical' under EPO practice.

The prioritizing step provides an advantage in that it can identify compounds having antibacterial activity and to which bacteria might not have evolved resistance. If the patent claim includes a step of obtaining a physical sample of the identified antibiotic, then the prioritizing step has a physical effect in the real world. This prioritizing step affects which compound is selected to prepare the physical sample. In other words, the step of obtaining the physical sample has the effect of 'anchoring' the computer-based prioritizing step in the real world.

But many applicants would prefer a patent claim that does not include a step of obtaining the physical sample of the identified antibiotic. They might prefer a patent claim that ended with a step of outputting a candidate compound on a computer screen. Getting a patent at the EPO for such a claim is more difficult, but could still be possible. The issue is whether a process that outputs the identity of a candidate compound, but does not provide a physical sample of that compound is itself 'technical'.

The same issue has been faced by engineers who increasingly use computer modelling to simulate physics as part of a design or development process. This is typical of work performed by modern engineers and the trend of recent case law in

Europe has been to accept that this work is technical in itself, essentially by virtue of it being the work carried out engineers, who are concerned with ‘technical’ matters almost by definition.

But the situation is still fluid despite this trend in case law because question has been referred to the EPO’s Enlarged Board of Appeal, i.e. the highest appeal body at the EPO. The Enlarged Board is currently deciding whether computer simulations are patentable by themselves or whether a final ‘anchoring’ step is needed.

The Enlarged Board is yet to issue a final decision so the situation is not confirmed either way. In the meantime it is important to file patent applications that are flexible enough to account for the uncertainty in this field.

Conclusion

Computer technologies such as AI are being used in fields far away from their computer science origins. In a few years’ time, drug discovery teams might look very different, most likely combining people with expertise in the life sciences and in electronics and computer science. We at Reddie and Grose, have formed a specialist interdisciplinary group with patent attorneys from backgrounds across these disciplines to assist our clients working at the cutting edge of technology where these fields converge. If you agree with us that AI and other computer technologies are going to become a big part of drug discovery in the coming years and would like to discuss how we can help you secure patents in this area, don’t hesitate to contact us.

Disclaimer

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